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CONTENTS

Hyaluronidase-sensitive mucopolysaccharide ..... *Lorenz E. Zimmerman* 1
Medullo-epithelioma ..... *Algernon B. Reese* 4
The trabecular meshwork ..... *František Vrabec* 7
Ophthalmology in a concentration camp ..... *Robert Salus* 12
Optic neuritis after chloramphenicol ..... *J. Gordon Cole, Helen Grady Cole and Lawrence A. Janoff* 18
Glaucoma detection in a general hospital ..... *John W. Smillie, F. Dale Roth, Fred Blum and L. Keith Gates* 20
Early diagnosis of primary glaucoma ..... *Winston Roberts* 24
The eye in old age ..... *A. L. Kornzweig, M. Feldstein and J. Schneider* 29
Pictures for preschool testing ..... *Henry F. Allen* 38
Ocular toxoplasmosis ..... *Sherman B. Forbes* 41
Effect of hypoxia ..... *John L. Brown, J. H. Hill and Richard E. Burke* 57
Senile spastic entropion ..... *Martin Bodian* 67
Topical anesthesia of cornea ..... *Thomas Behrendt* 74
Fuller-Albright syndrome ..... *Joseph E. Alfano* 77
Immunization against herpes keratitis ..... *R. Gispen* 88
Corticosteroids in aqueous ..... *Harry Green, Henry S. Kroman and Irving H. Leopold* 91
Biochemical studies on cataract ..... *S. Ogino, H. Tojo, I. Fujishige and Y. Katumori* 94
Spontaneous cyst of iris ..... *DuPont Guerry, III, and Herbert Wiesinger* 106
Monilia keratoconjunctivitis ..... *Shaler S. Roberts* 108
Jimson weed mydriasis ..... *F. H. Simmons* 109
Visual loss after quinine ..... *Charles A. Turtz* 110
Epiblepharon and entropion ..... *Jesse M. Levitt* 112

DEPARTMENTS

Society Proceedings 114 Obituaries ..... 129 Abstracts 135
Editorials ..... 125 Correspondence ... 131 News Items 156
Book Reviews 132

For a complete table of contents see page xxv

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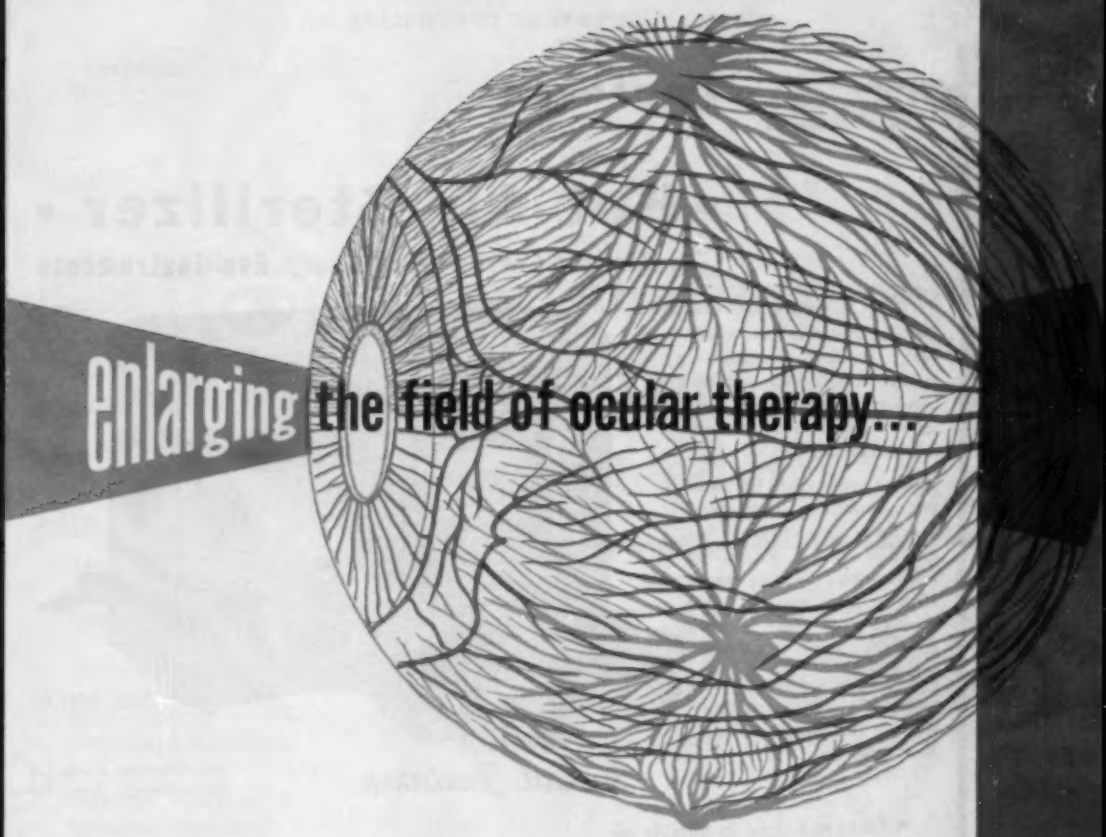

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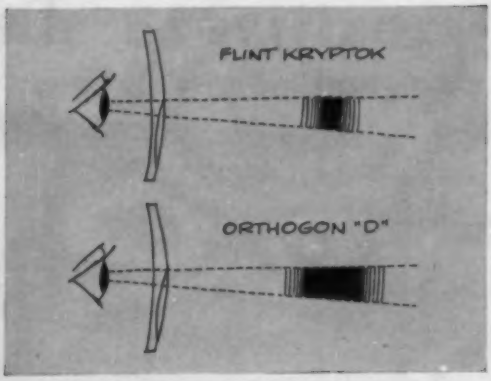

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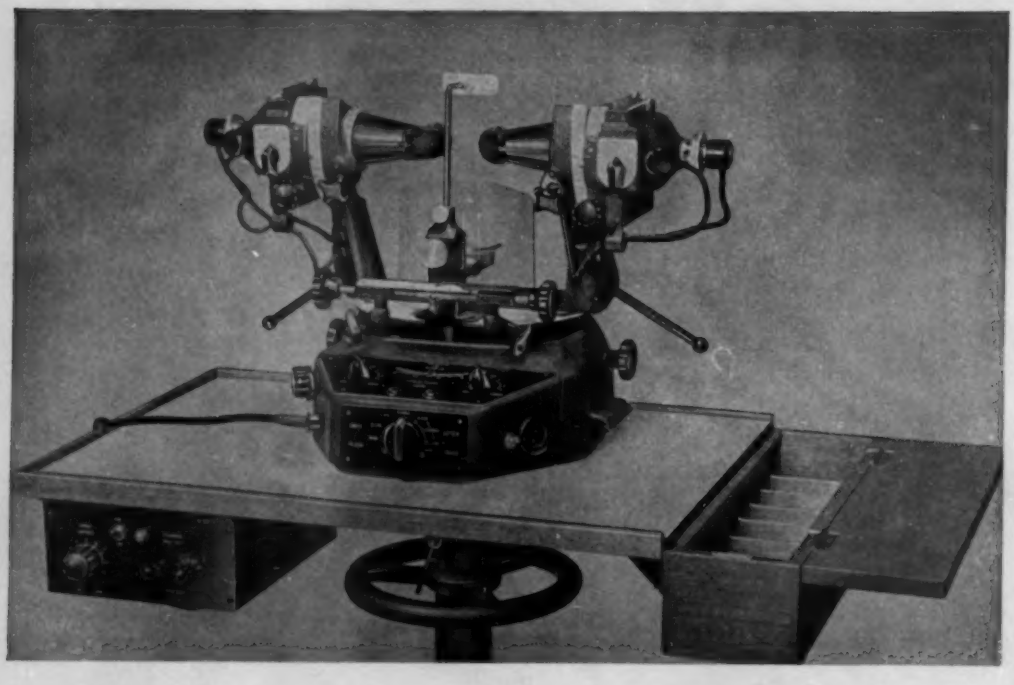

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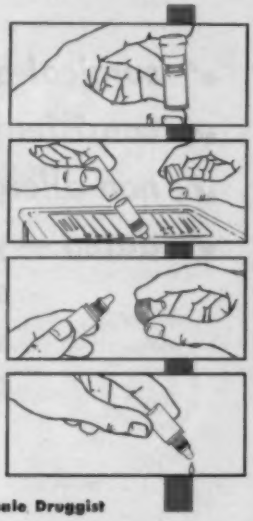

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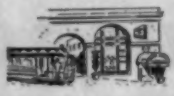

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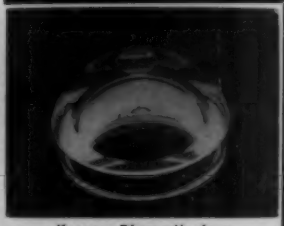

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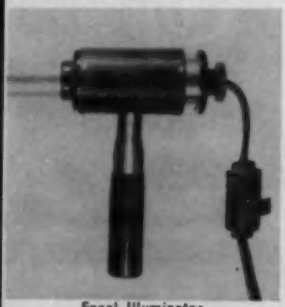

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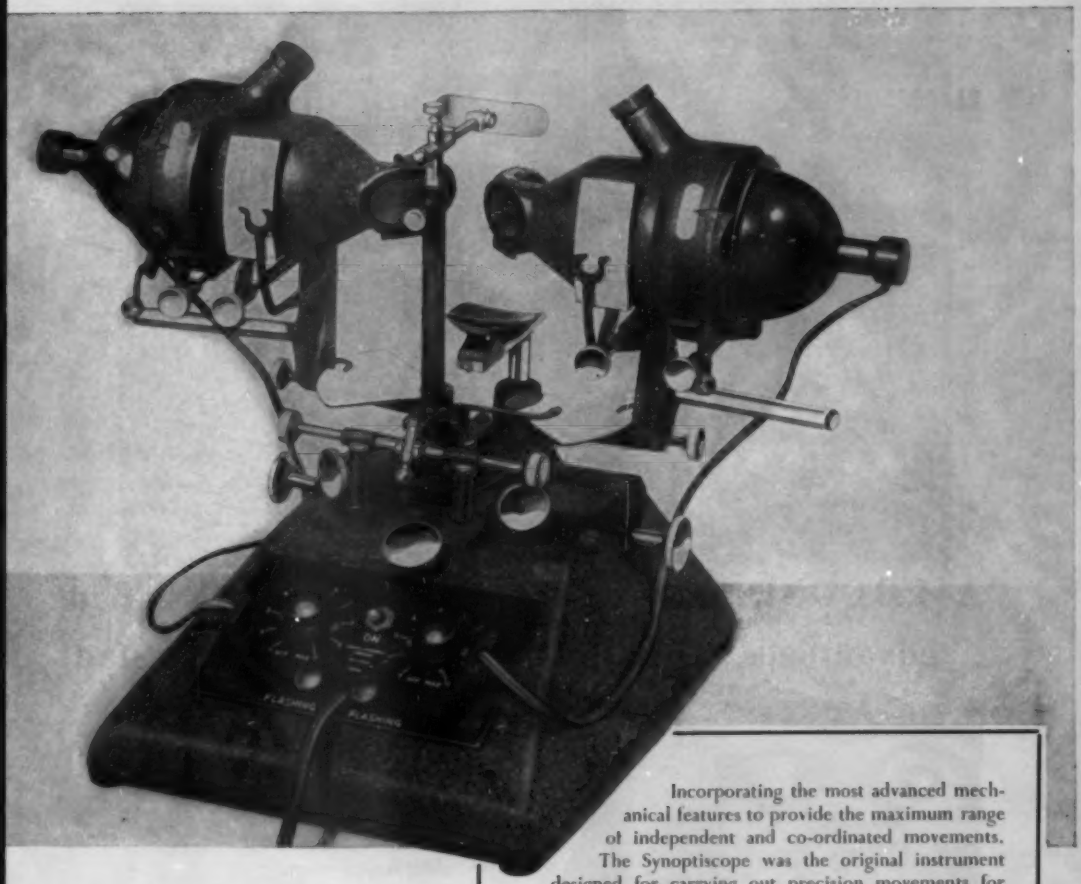

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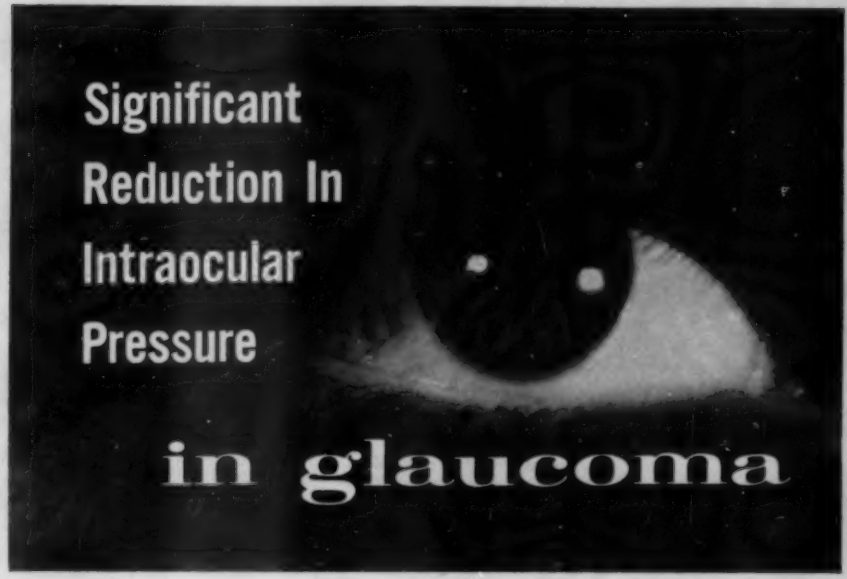

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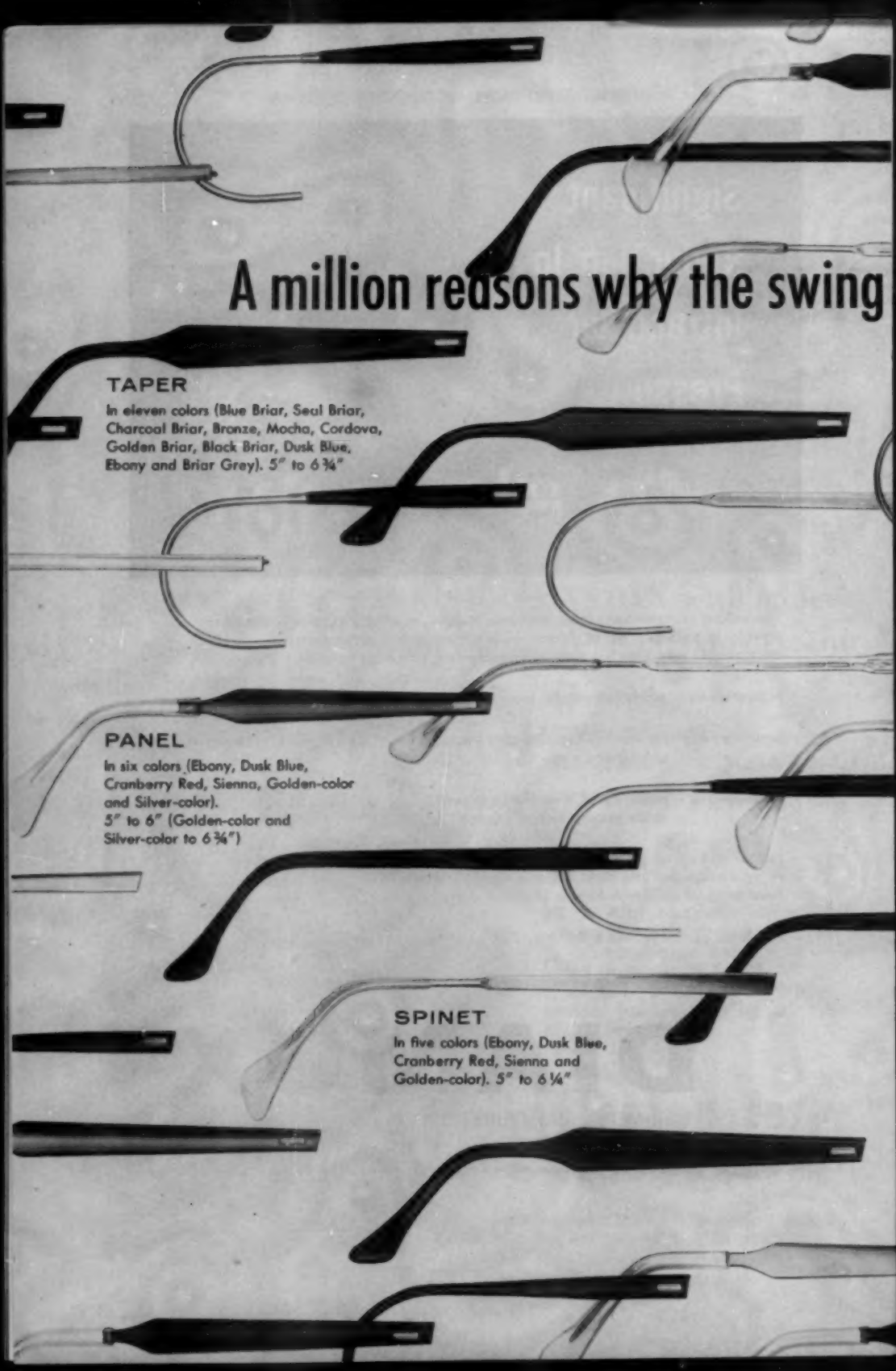
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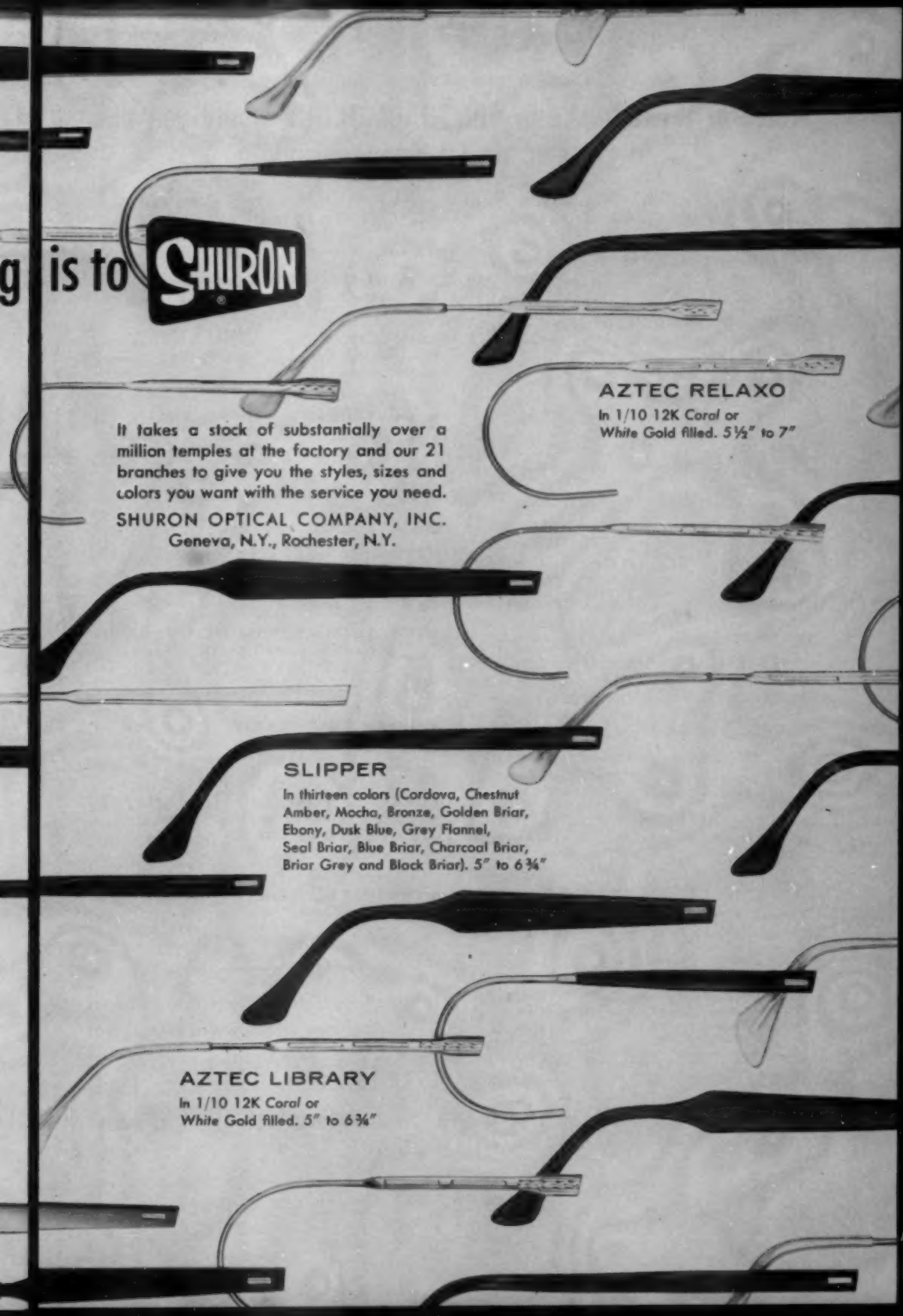

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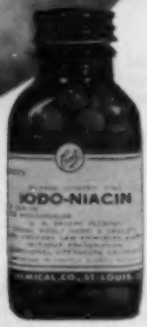

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1. *Cecil's Textbook of Medicine*, 7th ed., 1947, p. 1287.
2. *Ibid.*, p. 1598.
3. *Am. J. Ophth.* 42:771, 1956.
4. *Am. J. Digest. Dis.* 22:5, 1955.
5. *Med. Times* 84:741, 1956.

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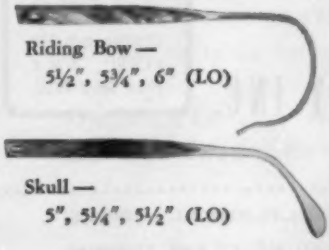

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SERIES 3 · VOLUME 44 · NUMBER 1 · JULY, 1957

CONTENTS

COLOR PLATE

Illustrating paper by Lorenz E. Zimmerman ..... *facing page* 1

ORIGINAL ARTICLES

Demonstration of hyaluronidase-sensitive acid mucopolysaccharide: In trabecula and iris in routine paraffin sections of adult human eyes: A preliminary report. Lorenz E. Zimmerman 1
Medullo-epithelioma (dictyoma) of the optic nerve. Algernon B. Reese 4
The inner surface of the trabecular meshwork studied by a replica technique. František Vrabec 7
Ophthalmology in a concentration camp. Robert Salus 12
A toxic ocular manifestation of chloramphenicol therapy: Report of a case of optic neuritis. J. Gordon Cole, Helen Grady Cole, and Lawrence A. Janoff 18
Glaucoma detection in a general hospital: A survey of 1,054 nearly consecutive admissions of patients over the age of 40 years. John W. Smillie, F. Dale Roth, Fred Blum and L. Keith Gates 20
Early diagnosis of primary glaucoma. Winston Roberts 24
The eye in old age: IV. Ocular survey of over one thousand aged persons with special reference to normal and disturbed visual function. A. L. Kornzweig, M. Feldstein and J. Schneider 29
A new picture series for preschool vision testing. Henry F. Allen 38
Ocular toxoplasmosis: Report of cases. Sherman B. Forbes 41
The effect of hypoxia on the human electroretinogram. John L. Brown, J. H. Hill and Richard E. Burke 57
A simple operation for senile spastic entropion. Martin Bodian 67
Experimental secondary effects of topical anesthesia of the cornea. Thomas Behrendt 74
Ocular manifestations of the Fuller-Albright syndrome. Joseph E. Alfano 77
Immunization against herpes keratitis in rabbits. R. Gispen 88
Corticosteroids in the aqueous humor of the rabbit eye: Further studies with paper chromatography. Harry Green, Henry S. Kroman and Irving H. Leopold 91
Biochemical studies on cataract: IX. Contribution to the histopathology of cataract caused by various quinoid substances. S. Ogino, H. Tojo, I. Fujishige and Y. Katumori 94

NOTES, CASES, INSTRUMENTS

Spontaneous cyst of the iris stroma. DuPont Guerry, III, and Herbert Wiesinger 106
Nystatin in monilia keratoconjunctivitis. Shaler S. Roberts 108
Jimson weed mydriasis in farmers. F. H. Simmons 109
Transient loss of vision following use of quinine. Charles A. Turtz 110
Epiblepharon and congenital entropion. Jesse M. Levitt 112

SOCIETY PROCEEDINGS

New England Ophthalmological Society, December 19, 1956 114
Yale University Clinical Conferences, February 10 and 24, 1956 118
College of Physicians of Philadelphia: Section on Ophthalmology, March 15, 1956 121

EDITORIALS

Spring meetings 1957 125
International Council of Ophthalmology 128

OBITUARIES

Arthur M. Yudkin 129
Harry Vincent Judge 130

CORRESPONDENCE

Viability of frozen corneas 131

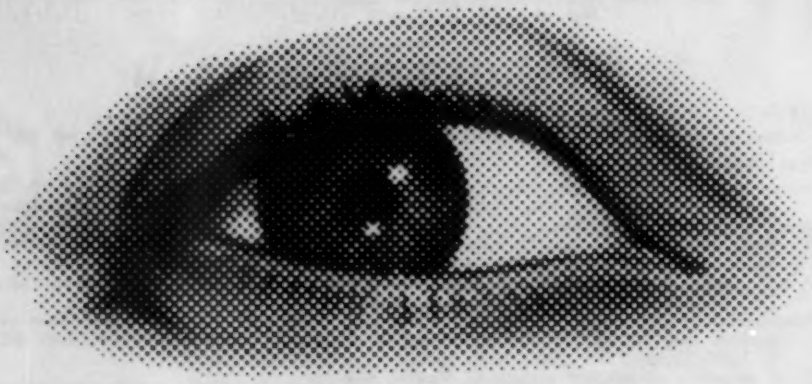
BOOK REVIEWS

Documenta Ophthalmologica 132
Connective Tissue in Health and Disease 132
The Year Book of the Eye, Ear, Nose and Throat (1956-1957) 133
Current Therapy: 1957 134
Optics: The Science of Vision 134

ABSTRACTS

Anatomy, embryology, and comparative ophthalmology; General pathology, bacteriology, immunology; Vegetative physiology, biochemistry, pharmacology, toxicology; Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses 135

NEWS ITEMS 156



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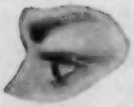

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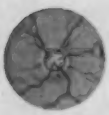

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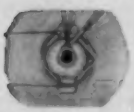

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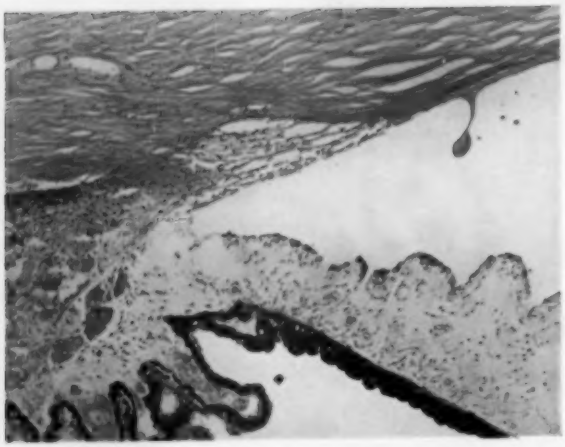
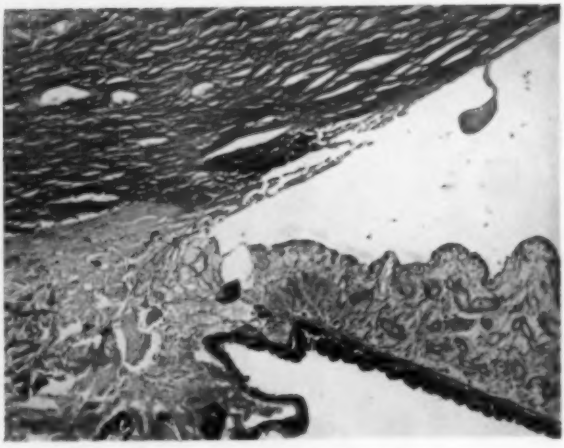
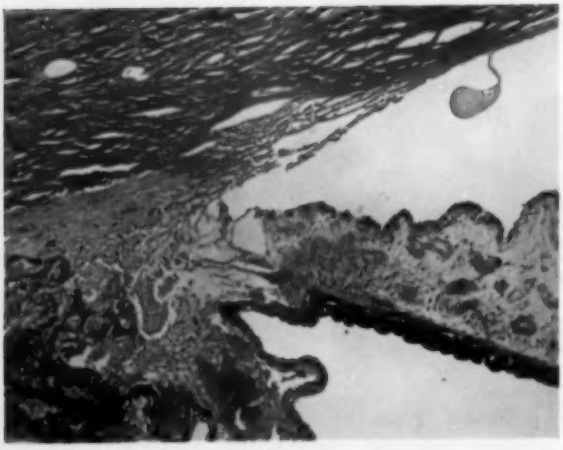


Fig. 1 (Zimmerman). This eye from a 66-year-old white woman was enucleated because of a small choroidal melanoma. The tension was 16.9 mm. Hg and the other eye was completely normal. (AFIP Acc. 758543. All illustrations magnified ×65.)

(A) The routine hematoxylin-eosin-stained section gives the impression that the intertrabecular spaces are empty. Observe also that the iris stroma and the uveal tissue in the chamber angle appear to contain an abundance of nonstaining ground substance.



(B) An adjacent section stained for acid mucopolysaccharides by the Rhinehart-Abul-Haj technic reveals much stainable material in the intertrabecular spaces and in the iris stroma. Acid mucopolysaccharides appear blue; collagen fibers stain red and the smooth muscles of the iris and ciliary body are pale yellow-green because of the picrofucsin counterstain employed.



(C) Another adjacent section has been stained by the same technic employed in B but the section was first treated with bovine testicular hyaluronidase. Now only a trace of the acid mucopolysaccharide remains in the intertrabecular spaces and none is observed in the iris stroma. This is histochemical evidence that an hyaluronidase-sensitive acid mucopolysaccharide is present in the trabecula and iris stroma.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 44 JULY, 1957 NUMBER 1

DEMONSTRATION OF HYALURONIDASE-SENSITIVE ACID MUCOPOLYSACCHARIDE*

IN TRABECULA AND IRIS IN ROUTINE PARAFFIN SECTIONS OF ADULT HUMAN EYES

A PRELIMINARY REPORT

LORENZ E. ZIMMERMAN, M.D.
Washington, D.C.

Hyaluronic acid is a mucopolysaccharide which in animal tissues seems to bind water in interstitial spaces. It holds cells together in a jellylike matrix and serves as a lubricant and shock-absorber.[8,9] The enzymes which hydrolyze or depolymerize hyaluronic acid are called hyaluronidases. Hyaluronic acid was first isolated from the vitreous. Subsequently, in 1936, it was reported to be present in the aqueous. In his fine review article of 1947, Meyer[8] presented evidence that hyaluronidase activity occurred within the aqueous in vivo and assumed that the depolymerized polysaccharide was removed through the normal exit channels of the eye. He even went so far as to suggest that "the cause of simple glaucoma may well be explained by inhibition of hyaluronidase in the eye."

More recently, Bárány[2] found that the addition of hyaluronidase to the perfusion fluid reduced by half the resistance to aqueous outflow of animal eyes. This effect was obtained in a matter of seconds. Bárány assumed that hyaluronic acid was present on the walls of the pores and channels between the anterior chamber angle and the canal of Schlemm. Although he was certain that the "angle tissue" contained "some metachromatic material," he stated that he could not locate the mucopolysaccharide with precision. Furthermore, he postulated that a layer of hyaluronic acid, not more than a 10th of a micron in thickness (and therefore invisible in ordinary histologic preparations), would still be capable of affecting aqueous outflow, as it does in normal eyes.

Very recently several workers have demonstrated histologically a metachromatic amorphous substance in the trabecular meshwork of human and animal eyes.[1,3,13] Brini observed that both the metachromasia and the alcian-blue staining were altered by hyaluronidase,[3] but his publication is not documented by photomicrographs. In Vrabec's paper there are photomicrographs which reveal an intense diffuse metachromasia of the trabecular meshwork of the sheep's eye, but precise histologic localization of the mucopolysaccharides in the drainage channels is not shown convincingly. However, Vrabec stated that all the spaces between the trabeculae seem to be filled by an amorphous substance which stains a reddish violet with cresyl violet.[13] To obtain these results he embedded his material in Celodal† having found fresh frozen sections and material embedded in paraffin or celloidin unsatisfactory. Brini, however, obtained satisfactory results with paraffin-embedding and he found the type of fixation unimportant.

* From the Central Laboratory for Pathologic Anatomy and Research, Veterans Administration, and the Armed Forces Institute of Pathology.

† Celodal, a product of Bayer, Leverkusen, is a clear thick liquid which polymerizes after the addition of acid substances.

The purpose of this communication is to present further evidence that the precise localization of an abundance of acid mucopolysaccharide, sensitive to hyaluronidase, can be demonstrated within the intertrabecular spaces in routine meridional sections of the surgically enucleated adult human eye, fixed in aqueous formalin, and embedded in paraffin. This demonstration may be accomplished with alcian blue,[7, 10] but, in my experience, the most striking preparations are obtained when the histochemical method described by Rhinehart and Abul-Haj[11] is used. Their technique is based on the principle first applied by Hale[6] in staining mucinous elements of connective tissues; that is, the affinity of acid mucopolysaccharides for colloidal iron. This makes it possible to demonstrate acid mucopolysaccharides by the Prussian blue reaction which causes them to appear bright blue in the final preparations. A picrofuchsin (Van Gieson) counterstain gives an effective contrast: collagen stains bright red, elastic fibrils and Descemet's membrane vary from yellow-orange to orange-brown, smooth muscle is greenish yellow, and nuclear chromatin gray-brown to gray-green.

The application of the Rhinehart-Abul-Haj technique to routine paraffin sections of formalin-fixed adult eyes enucleated because of choroidal melanomas* clearly demonstrates the presence of an abundance of acid mucopolysaccharide within the spaces between the corneoscleral trabeculae (fig. 1-B). This mucoid material is sometimes visible in routine hematoxylin-eosin-stained sections as a very faint grayish film, but usually the intertrabecular spaces appear empty (fig. 1-A).

In appropriately stained sections the acid mucopolysaccharide appears to be most abundant in that part of the trabecular apparatus adjacent to the inner wall of Schlemm's canal. This is the "pore area" to which Flocks has called attention.[5] In tangential sections through the trabecula and, in fact, in routine sections also, the trabecular fibers are much finer and the channels more cellular in the "pore area" than elsewhere. The seemingly smaller amount of polysaccharide in those spaces close to the anterior chamber may be artefact. Here the spaces are larger and the tissue less cellular; thus the polysaccharide could be dissolved or dislodged from the area. The very thin film of mucopolysaccharide that remains clinging to the surface of the coarse corneoscleral trabeculae adjacent to the anterior chamber suggests that more polysaccharide had been present in vivo. Acid mucopolysaccharides also fill the loose, pale-staining (with hematoxylin-eosin) uveal tissue of the angle anterior to the ciliary muscle and are abundant in the iris stroma (fig. 1-B).

The specifically stained acid mucopolysaccharide that fills the intertrabecular spaces and is present throughout the loose stroma of the iris and anterior chamber angle can be removed by pretreatment of the paraffin sections with commercial frozen-dried bovine testicular hyaluronidase* (fig. 1-C). It is presumed, therefore, to be an hyaluronic acid.

In the course of these histochemical studies a number of other observations were made; one of particular value to the immediate discussion is that the vitreous and the layer of rods and cones will serve as control tissues for evaluation of the histochemical reactions. It is well known that an abundance of hyaluronic acid is present in the normal vitreous.[8] This substance can be stained by the Rhinehart-Abul-Haj technique and can also be removed by pretreatment with hyaluronidase. A relatively insoluble carbohydrate conjugated with either protein or lipid, or both, is known to be localized to the outer segment of rods of all species and cones of some species.[12] When stained for acid mucopolysaccharides, this carbohydrate

* The anterior segment of these eyes was considered normal, and clinically there was no evidence of glaucoma, uveitis, or other complicating disease.

* Wydase®, Wyeth.

gives an intensely positive reaction (deep blue stain) which is not altered by pretreatment with hyaluronidase.

Comment

We can only speculate as to the physiologic significance of the hyaluronidase-sensitive material in the trabecular spaces, for so little is known of the function of acid mucopolysaccharides. The fact that these substances are flexible chain polymers of high negative charge, with an affinity for cations and water molecules, suggests that they may play a critical role in regulating the metabolism of inorganic ions and water. A change in the concentration or the molecular size of such a substance might be of great importance in modifying the capacity of connective tissue to bind water and salts.[4] In addition to its water-binding property (and possibly because of this characteristic), hyaluronic acid seems to serve as a lubricant and shock absorber. The structure of hyaluronic acid as a highly hydrated coiled sphere, easily deformed by flow and easily "drained," appears to explain these biologic functions.[9]

The presence of hyaluronic acid between the corneoscleral fibers of the drainage channels might serve a dual purpose. On the one hand, its concentration and degree of polymerization probably influence the facility of aqueous outflow, as Bárány has demonstrated by perfusion experiments in animals. On the other hand, the shock-absorbing and lubricating functions of hyaluronic acid might be important in keeping open the exit pathways between the anterior chamber and the canal of Schlemm. Thus, in an acute experiment, the removal of hyaluronic acid by perfusion with hyaluronidase might lower the resistance to aqueous outflow, while the persistent absence of mucopolysaccharide from the intertrabecular spaces might lead to the development of increased resistance. In fact, Bárány has shown (by animal experimentation) that the removal of hyaluronic acid by injection of hyaluronidase into the anterior chamber in vivo is followed by return of "normal" resistance within four hours. This new resistance, however, is temporarily insensitive to hyaluronidase; that is, the temporary compensatory resistance that develops is not dependent on hyaluronic acid. Possibly, if injections of hyaluronidase into the anterior chamber were repeated over a long period of time, the nice homeostatic balance might be upset and excessive resistance to aqueous outflow might develop.

The histologic demonstration of an abundance of hyaluronidase-sensitive acid mucopolysaccharide in the iris stroma might arouse speculation as to whether the lowered resistance obtained by Bárány when he perfused the anterior chamber with hyaluronidase might not be the result of escape of fluid through the iris. Bárány, himself, considered this possibility, but he believed his results to be "incompatible with the assumption of independent extra channels being opened, but fits with an arrangement of the hyaluronidase-sensitive material on the walls of the pores and channels."

The source of the hyaluronic acid in the trabecula is unknown. Two theories deserve primary consideration. It is generally believed that the mucopolysaccharides of ground substance are derived from mesenchymal cells. Hence the endothelial cells covering the trabecular fibers might secret the intertrabecular mucous substance. On the other hand, this material might be derived from the aqueous, since the latter is known to contain hyaluronic acid. It is conceivable that these large molecules of highly polymerized mucopolysaccharide are filtered out of the aqueous by the trabecula. Bárány favored this concept, for he found the resistance rose when he perfused the eye with high-molecular hyaluronic acid, but fell when he used a solution containing no hyaluronic acid. Perfusion with cattle aqueous that had been boiled and spun in the ultracentrifuge maintained the normal resistance of the chamber angle. The hyaluronic acid of the

iris stroma may also be derived from the aqueous, for plasma proteins and specific cell types observed in the aqueous in various pathologic conditions are often also found in the iris stroma. The possibility that stromal cells of the iris can produce a ground substance of hyaluronic acid must be considered.

SUMMARY

The presence of hyaluronidase-sensitive acid mucopolysaccharide has been demonstrated in the intertrabecular spaces and iris stroma of adult human eyes fixed in aqueous formalin and embedded in paraffin.

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MEDULLO-EPITHELIOMA (DICTYOMA) OF THE OPTIC NERVE*

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A medullo-epithelioma (dictyoma) arising from the ciliary body is an accepted, although extremely rare, occurrence. That such a tumor may arise in the optic nerve is not known, so far as I can tell, and therefore I should like to put on record such a case.

A boy (D. S.), aged four and one-half years, was noted to have a drooping left upper lid in January, 1955. Upon covering the fellow eye it was found that there was no vision in the left eye. An examination in March, 1955, revealed a marked swelling of the left disc and no light perception. An astrocytoma (glioma) was suspected and X-ray films showed the left orbit and optic canal a trifle larger than the right. A question arose among the roentgenologists as to

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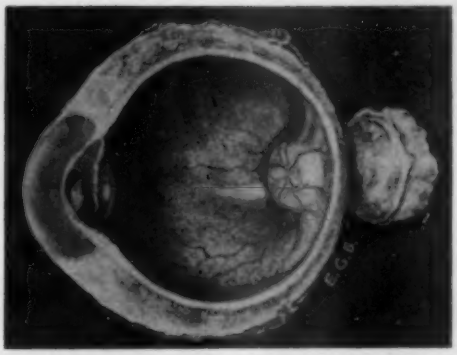

Fig. 1 (Reese). A calotte has been removed from the enucleated globe and the enlarged optic disc can be seen as well as the severed optic nerve.

whether or not the difference in the size of the two canals was significant. There was no exophthalmos—a feature thought to be unusual for astrocytoma.

By July, 1955, the swelling of the left disc had progressed tremendously and there was a one to two mm. exophthalmos. The disc lesion manifested itself as an enormous white globular mass (fig. 1). The right eye revealed no pathologic alteration and the central and peripheral fields were normal.

The left eye was enucleated by Dr. F. Jason Crigler and at the time of the operation palpation revealed that the tumor extended to, and probably through, the optic foramen. Therefore, a short time later the optic chiasm was exposed through a transcranial approach. As the intracranial portion did not seem to be involved, the optic nerve was severed close to the chiasm, the optic foramen opened, and the remainder of the nerve removed.

Nine months later a mass was noted in the orbit and biopsy revealed that it was recurrent tumor. From our studies we concluded that the tumor had extended intracranially and that the cranial extension, as well as the orbital recurrence, should be removed.

Dr. Joseph Ransohoff performed a left frontal craniotomy, retracted the frontal lobe and, by an extradural exploration, found tumor deep around the sphenoid ridge and extending through the defect in the roof of the orbit. At this point Dr. Ira S. Jones performed an exenteration of the orbit. The operation was continued further by Dr. Ransohoff who performed a gross total removal of the tumor mass by freeing it from its dural attachment and checking by frozen biopsy sections whether the dissection was beyond tumor extension.

In the following two months the patient received 5,200 r in air to the orbit. Also, he had two doses of triethylenemelamine (1.5 mg.) intramuscularly.

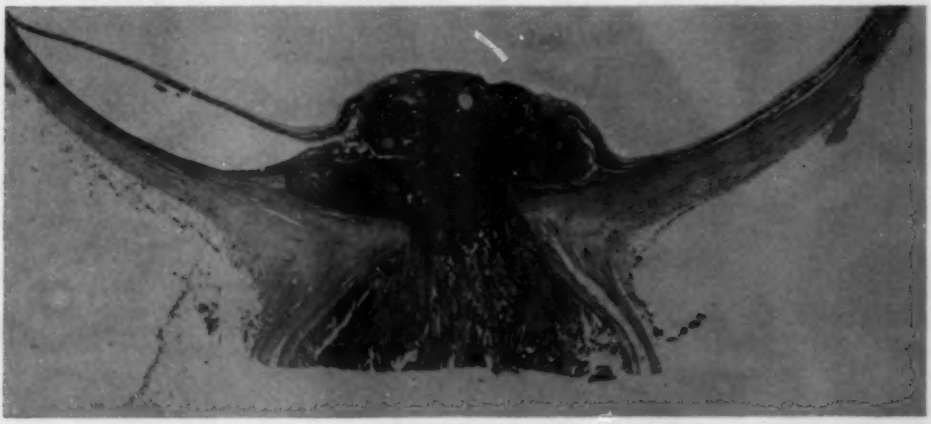

Fig. 2 (Reese). Cross section of the involved optic nerve (hematoxylin and eosin stain).

Fig. 3 (Reese). Characteristic area of the tumor (hematoxylin and eosin stain).

Fig. 4 (Reese). High power of a portion from the upper center (hematoxylin and eosion stain).

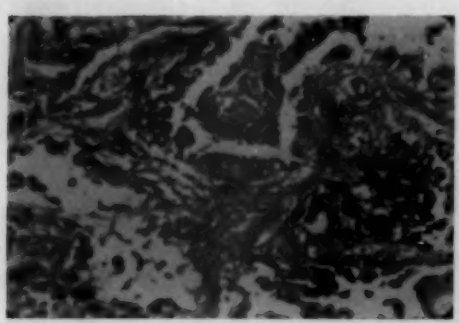

Fig. 5 (Reese). An area of melanin formation as shown by the Fontana stain.

Pathology

The tumor replaces the optic nerve (fig. 2) and protrudes some distance toward the vitreous. The structure is that of embryonic retina with a general pattern of the primary and secondary optic vesicles (figs. 3 and 4). In some places a structure resembling the inner layer of the vesicle predominates even to rudimentary rods and cones and in others the outer layer is in the ascendency. At sites in the vesicle there is fine fibrous connective tissue with, perhaps, blood vessels and this is interpreted as the analog of primary vitreous. Rarely, the tumor grows as a single layer of epithelium.

Besides the hematoxylin and eosin stain, tetrachrome, reticulin, and Fontana stains were done. The Fontana stain brought out areas of melanin (fig. 5) produced by tumor cells which had declared themselves to be the outer layer of the optic vesicle and were, thus, abortive pigment epithelium.

Discussion

This case is reported as an oncologic oddity. It is not recorded as a cure although now, after eight months have elapsed since the last surgery, no evidence of this rapidly growing tumor has manifested itself.*

I do not know how this tumor could be differentiated clinically from an astrocytoma. An astrocytoma grows much slower and is frequently associated with some early sign of neurofibromatosis (café au lait pigmentation).

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* In January, 1957, recurrences were noted in the bones of the orbit. A radical resection was done by Dr. John J. Conley which included the bones about the orbit and the associated soft tissues, that is, a portion of the frontal bone, frontal sinuses, ethmoids, cribriform plate, bony base of the skull in the frontal area, sphenoid, ascending crest of the maxilla, maxilla, malar compound zygoma, and infratemporal fossa along with the pterygoid plates. After four months' time, there is no evidence of recurrence.

THE INNER SURFACE OF THE TRABECULAR MESHWORK STUDIED BY A REPLICA TECHNIQUE*

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I. INTRODUCTION

The histologic structure of the meshwork of the angle of the anterior chamber has been described in full detail in the work of earlier and recent authors (Asayama, 1902; Lauber, 1902; Virchow, 1910; Rochon-Duvigneaud, 1943; Dvorak-Theobald, 1955; Ashton, Brini, and Smith, 1956; Rohen, 1956). Most of these investigators have tried to convey a mental image of the meshwork by combining the details of sections oriented in all three spatial directions. Some authors (Dvorak-Theobald, for example) have worked by the very expensive method of plastic reconstruction in attempts to establish the connections of the canal of Schlemm with the anterior ciliary veins and with the anterior chamber. Interesting and detailed as these papers are they do not present a sufficiently plastic image of the inner surface of the scleral meshwork.

Many earlier authors (Iwanoff and Rollet, 1869; Rochon-Duvigneaud, 1892-93; Asayama, 1902; Virchow, 1910) had used the direct method of observation of the surface of the trabecular meshwork but their observations were limited by the very low magnification they were able to use.

Findings based on the replica method are now presented. This method has proved to be generally useful in the study of uneven surfaces. I have used it in the past with satisfactory results in connection with the endothelium on the surface of the iris (Vrabec, 1952).

II. MATERIAL AND METHODS

Three human eyes with normal anterior segments and many eyes of various mammals and birds were used. The material is fixed fresh in 10-percent neutral formol for a few days or weeks. The anterior segment is then divided into four quadrants, and rinsed in tap water for 20 to 30 minutes. The iris and ciliary body are then carefully removed from the sclera and cornea by gentle traction in an equatorial direction.

The piece of sclera and cornea is placed on a filter paper with the inner surface up, and the inner surface is blotted very gently three times with a smooth filter paper. The tissue is then allowed to dry for about two minutes at room temperature, and the surface is coated by means of a soft camel-hair brush with a thin layer of a five-percent solution of methyl methacrylate in chloroform.

After 20 to 30 seconds, a piece of adhesive cellophane tape is gently pressed onto the dry methacrylate surface. The replica adheres to the tape, and can be removed and mounted on a glass slide with the replica facing downward and protected by the tape.

The technique is so gentle that four or five replicas may be stripped from the same surface without apparent damage. In fact, the second and third replicas were found to be better than the first, possibly because of the removal of some water. Consequently three replicas were made of every specimen.

The replicas should be viewed in oblique illumination, which clearly shows up the relief.

As the replicas are very faithful, high-power lenses may be used in studying them. To begin with most observers experience some difficulty in interpreting these preparations, since the images are three dimensional.

FINDINGS

The following method of observation is recommended:

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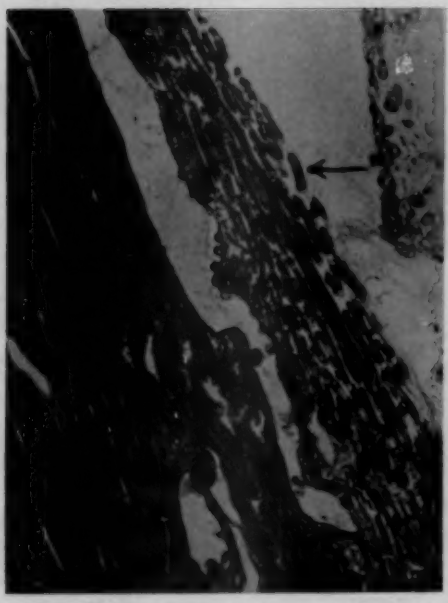

Fig. 1 (Vrabec). Sagittal section through the human anterior chamber angle. The loose inner trabeculas are clearly seen (at arrow). The external layers show a more compact structure. (×100, Heidenhain iron-haematox.)

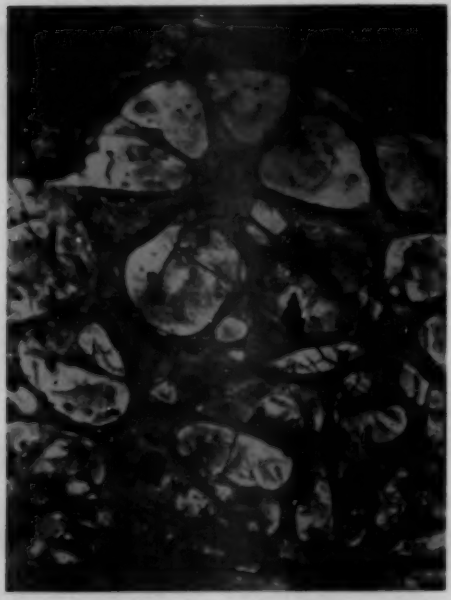

Fig. 2 (Vrabec). Flat frozen section of the human trabecular meshwork, silver impregnated by the Gros-Schultze method. Steilate anastomoses of the inner trabeculas with large meshes through which smaller holes of the external trabeculas are seen. Some nerve fibers pass the meshwork. (×100.)

Fig. 3 (Vrabec). Methyl methacrylate replica of the inner surface of the human trabecular meshwork (♂, 10 years old). The tissue was incubated in hyaluronidase solution after formol fixation, in order to bring out more detail. Loose inner trabeculas forming large meshes and external trabeculas with rounded holes. The meridional direction is indicated by arrow. (×100, oblique illumination.)

Using a low-power objective, identify the corneal endothelium—this presents no difficulty even to an untrained observer—(fig. 6-A). By moving toward the periphery of the cornea, it is then practically impossible to miss the intermediary zone (fig. 6-B) between the corneal endothelium and the meshwork.

This zone is generally poor in detail. It forms the transition to the meshwork. The meshwork extends over a space varying in

width according to the species of animal and the meridian of the eye.

In mammals other than primates, it is useful to subdivide the inner surface of the scleral meshwork into two zones: the first of them, following immediately on the intermediary zone, contains broad trabeculas, the second only narrow ones. In both zones the trabeculas mainly run in an equatorial direction. In the second zone, endings of the tendons of the ciliary muscle can sometimes be seen running meridionally. The trabecular meshwork ends very abruptly and the inner surface of the sclera with fine fibrils and bundles arranged meridionally presents the last point of orientation.

Consequently, we prefer the following division of the inner surface of the corneoscleral region: (1) Corneal endothelium, (2) intermediate zone, (3) region of broad trabeculas, (4) region of narrow trabeculas (the last two zones useful only in orders of mammals other than primates), and (5) the inner surface of the sclera.

1. Corneal endothelium

This shows various pictures depending mainly on the technique used. As a rule the intercellular cement lines and the contours of the nuclei are only indistinctly seen. On the surface of the endothelium parallel wrinkles suggesting the existence of a superficial layer of some substance are sometimes seen.

2. The intermediate zone

Artefacts seem to be particularly frequent in this one. The endothelium, being too thin and flattened in this region, obviously cannot stand the mechanical insults of the replica method. Nevertheless, careful technique, avoiding strong pulling, results in beautiful pictures of this zone with conservation of all fine details. It is then possible to see how the endothelial cells elongate in the meridional direction and then disappear (fig. 6-B1). Then come the meridional trabeculas (fig. 6-B2) which, as is evident from the sagittal histologic sections of this region, emerge from the anterior surface of the periphery of Descemet's membrane. Toward the trabecular meshwork they very often end in a broad flat circular band (fig. 6-B3) and only very few of them can be traced across this zone in a meridional direction.

The flat circular zone appears to be very irregularly developed, and varies within broad limits even within individual eyes. It seems to represent the anterior ring of Schwalbe. The details of the intermediary zone are rather indistinct as though covered by a thin film of some amorphous substance similar to that observed on the corneal endothelium. Digestion with testicular hyaluronidase brings out more detail (figs. 5 and 6).

Immediately behind this region begins:

3. The trabecular meshwork

The most striking feature of this region is the species variation. In man, and perhaps in other primates, the two distinct zones found in other mammals are very poorly defined. The inner surface of the meshwork shows firstly the thin round trabeculas the direction of which appears to be chiefly meridional; these branch and anastomose to form a loose network of coarse meshes slightly elongated in the meridional direction (fig. 3). The looseness of the inner layer of the trabecular meshwork appears also in normal histologic sections (figs. 1 and 2).

More posteriorly even the inner trabeculas tend to lie in a more equatorial direction. Here in the posterior zone of the meshwork the inner layer of trabeculas is sometimes accidentally removed exposing the external layers. These external trabeculas tend to widen into broad sheets with oval or round perforations (fig. 3). The structure of the bundles and plates is fibrillar; and is more clearly seen after the action of hyaluronidase. Hyaluronidase also shows up more clearly the perforations which are otherwise seen to have indistinct slanting borders (figs. 5 and 6). It should be mentioned, however,

Fig. 4 (Vrabec). Replica of the inner surface of the scleral trabecular meshwork of the cat. Meridional direction indicated by arrow. All the trabeculas and holes are elongated in the meridional direction. (×100.) The carnivores form an exception to the rule mentioned in the text.

Fig. 5 (Vrabec). Replica of the peripheral corneal endothelium and the intermediary zone in the human eye (same as Figure 3). Endothelial cells are seen somewhat indistinctly, as are the details of the intermediary zone. The sharp boundaries of some tissue particles (arrow) indicate that the focussing was sharp. (×100.)

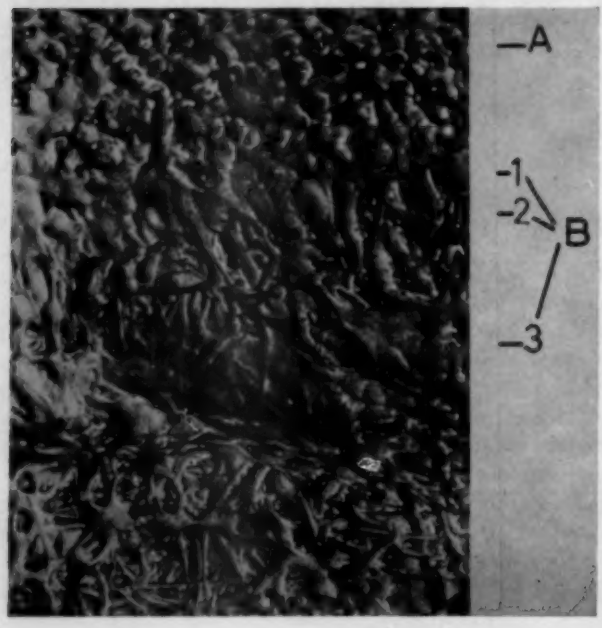

Fig. 6 (Vrabec). Replica of the contralateral part of the trabecular meshwork in the same human eye, incubated in hyaluronidase for three hours after formol fixation. (Testicular enzyme, Hyasa, of Czechoslovakian manufacture, 150 units in two ml.) The details are seen more distinctly than in the previous picture. (A) Endothelium. (B) Intermediate zone. (1) Transition of endothelium into the intermediate zone. (2) Meridional trabeculas passing in front of Descemet's membrane. (3) Anterior ring of Schwalbe. Some endothelial-cell nuclei are visible at arrows (×100.)

that one generally gains the impression of a thin layer of some substance persisting even after prolonged incubation with hyaluronidase.

The trabecular meshwork in other mammals appears to be subdivided into two other zones. The first of them, immediately following the intermediate zone, shows broad trabeculas or plates with equatorially elongated perforations. The more posterior second zone exhibits thinner trabeculas also running in an equatorial direction. Here, in the second zone, the anterior endings of the tendons of the ciliary muscle are most frequently seen—thin, round, meridional bundles, splitting into branches and then bending equatorially to end with many arborizations on the trabeculas. See Figure 4 in the present paper and Figures 3 and 6 in the succeeding one by Berggren and Vrabec.*

In birds there are many thin uveal trabeculas on the inner surface of the scleral meshwork; and here, too, the broad external trabeculas are seen to be coated with the amorphous substance.

5. The inner surface of the sclera

Moving still farther backward a sudden change takes place. The circular pattern of the trabecular meshwork is relieved by a strictly meridional orientation of all elements. All the replicas show single fibrils or bundles of them—very thin, isolated, sometimes branching fibrils or bundles of wavy fibrils which never branch (the latter show the very typical pattern of large collagen bundles). It is impossible even for an untrained observer to miss this sudden change of the picture.

III. Discussion and Conclusions

It has been shown that by the replica method the surface anatomy of the trabecular meshwork can be studied in detail. The main findings of this study are not different from those obtained by specialists on this region. However, this method, in addition to its simplicity, has the advantage of revealing more fully the entire inner surface of the scleral trabeculas as an anatomic unit. This gives a better understanding of the "functional adaptations."

The decisive advantage of the technique lics in the possibility of taking replicas of moist surfaces, where the very sensitive gelatinous coating on the endothelial lining of the structures can be demonstrated. This jellylike substance, the presence of which was suspected by Virchow, had never previously been demonstrated conclusively, although its existence had been proved using physiologic methods by Bárány in 1953-54 (see Bárány, 1956, for references) and confirmed by François, Neetens, and Collette (1956) in microradiographic experiments.

Morphologic evidence of the existence of the substance is still very difficult to obtain by classical histologic methods, however, mainly because of the high content of water. I believe that the substance is closely related to the metachromatic substance demonstrated on the surface of vascular endothelium and mesenchymal epithelium (peritoneal) by McGovern (1955-56). Wolf (1956) in his study of endothelium based on the histology and electron microscopy of this tissue also suggests the existence of such a covering substance.

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* Berggren, L., and Vrabec, F.: Demonstration of a coating substance in the trabecular meshwork of the eye and its decrease after perfusion experiments with different kinds of hyaluronidase. To be published in The Journal in August, 1957.

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OPHTHALMOLOGY IN A CONCENTRATION CAMP

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Translated by STEFAN VAN WIEN, M.D., *Chicago, Illinois*

Of all the professional people who had to live and work in the hell of concentration camps, physicians showed the highest morale.

Frequently separated from their families and ejected from their accustomed routine and secure position, they were thrown into an adventure whose tragic ending could have seemed doubtful only to the most confirmed optimists. Yet, without exception, physicians accepted their lot and overcame almost superhuman obstacles until their stamina gave out. A great many physicians, old and young, and representing all specialties were deported to concentration camps. Still, in proportion, there were too many patients for the number of physicians. For everybody became ill after only a few weeks in a camp. To give medical help or even moral support to the unending stream of diseased persons really taxed to the utmost the physical and spiritual strength of the physician. He had to overcome all sorts of obstacles—including his own physical and mental distress.

The camp in which I lived and worked for more than two years was formerly populated by a few thousand inhabitants but then housed about 40,000 and, at times, as many as 60,000 people. It had to be expected that, in spite of all medical precautions and the best hygienic measures possible under such conditions, there would be instances of contagious diseases among a crowd of desperate and ruthless human beings. This was particularly true for the many old and fragile inmates, some of them ill before they arrived. At one time or another, there were cases of typhoid fever, dysentery, encephalitis, typhus, tuberculosis, and so forth.

At first, our specialty was well represented. The equipment of deported physi-

cians was used in these camps, so our armamentarium was relatively good. There was even an optical institute with a bare minimum of equipment. Ophthalmologists worked in several dispensaries. In a central eye department, patients who had to be hospitalized were cared for. The work, including the surgery, was very similar to that in any clinic.

Most cases were routine and of no particular interest. Some common diseases were conspicuous by their unusually severe course. I mention here numerous cases of glaucoma (especially in the fall and winter) that could rarely be controlled with conservative measures. They had to be operated during the acute stage, as a rule with satisfactory results. Some cases of keratitis that initially appeared quite harmless, suddenly assumed a malignant course. I shall later discuss the causes for this phenomenon.

I saw other diseases in much greater number than either before or after my experience in the camp. I mention as an example the enormous number of cases of epidemic keratoconjunctivitis. Their clinical appearance and course were similar to that seen in the epidemics in Vienna, Cologne, and elsewhere a few years ago. Now and then, during peace time, I have seen cases that more or less resembled the picture described in the literature as epidemic keratoconjunctivitis. We called it Fuchs' keratitis subepithelialis punctata; however, these were isolated instances without epidemic occurrence.

In the camp, the epidemic character was so marked that there were times when not a day passed without new cases coming in for treatment. The initial stage was a more or less acute conjunctivitis. After this acute stage subsided, small round coin-shaped (thus the former term "keratitis nummularis Stellwag"), subepithelial grayish punctate infiltrates appeared that caused a cushionlike elevation of the epithelium. At times the infiltrates were isolated but, in severe cases, they were so numerous that the entire cornea was covered by them and appeared cloudy. Occasionally one eye, but more frequently both eyes, were involved. There was considerable subjective discomfort only in the acute stage. In the chronic stage, there were moderate visual disturbances in the more severe cases that eventually improved. But even to this day, I know of a few cases that distinctly show some of the characteristic round spots. Systemic treatment was not very satisfactory. Sulfonamides were of doubtful value. Among the drugs for topical application that were available, methylene blue (Merck) seemed to be best in the acute stage. Antibiotics were unknown to us at that time.

There was almost complete isolation in the camp in intellectual, especially medicoscientific, matters. We had no knowledge of what was happening in the outside world. The only form of correspondence permitted consisted of postcards with a printed message stating that the sender was well and bearing his signature. Some time before I arrived at the camp, several young people had been publicly executed for writing letters to their closest relatives.

It is understandable that everyone had a burning desire to get the latest news about the war. We all knew that our only hope to leave the camp alive was the earliest and complete defeat of the Nazis. Some daring fellows had mysterious means of obtaining newspapers. These papers, always quite old, were either in German or Czech and contained only the official reports of German victories. These reports were the basis for rumors that were either optimistic in the case of setbacks for the Nazis or pessimistic in the case of their successes. As a rule, the rumors were false; eventually one became morose and did not believe any of them.

In spite of our efforts to combat epidemic keratoconjunctivitis, it seemed to spread at first but, then, ceased rather suddenly. Encephalitis was another disease that took on epidemic proportions. Its ophthalmologic manifestations were nystagmus, convergence insufficiency, exotropia, and occasionally,

pareses of the lateral recti and elevator muscles. We frequently came across cases with a bilateral superior rectus paresis or diplopia suggesting such a cause. I believe they could be explained on the basis of convergence insufficiency or exotropia that would assert itself more in extreme elevation than in depression. Ophthalmoscopic findings usually were normal. The prognosis was generally favorable; to the best of my knowledge, most cases recovered without residua after a few months.

The incidence of herpes zoster ophthalmicus was no greater than elsewhere. Except for one single case of an old cicatricial trachoma, this disease did not exist in our camp.

Other conditions of interest to the ophthalmologist were closely associated with the dietary situation. When I arrived at the camp in mid-1943, the worst hunger period of 1941 and 1942 was over, at least as far as the quantity of food was concerned. The quality was the worst that could be imagined. In our camp, as in others, food was assigned by the SS commander of the camp according to the number of inmates and based on "certain norms" of the "nutritional state." The basic caloric value of the rations for those who did not work or who did only light work was between 1,400 and 1,500 calories. For those who did heavy work, it was about 2,000 calories, that is, a little more than half the scientifically calculated requirements. However, these figures were only on paper. They were the amount of food supposedly issued by the camp command, not considering the loss in preparation of the food, and not taking into consideration the loss caused by those who handled and distributed the food and whose craving stomachs were also empty.

When the food reached the consumer, it had only a fraction of its original value. The choice morsels had disappeared en route from the kitchen to the table. Meat, for example, was served once or twice a week. It came from diseased and condemned cattle. It was of the worst quality, often ill smelling. It was counted at its full caloric value (about 160 to 200 per 100 gm.; this may have been correct at the time of the processing). By the time it was served, it contained hardly one tenth of its original value. It consisted of a brownish concoction called goulash. If one was lucky, he occasionally found a few solid pieces of tough and indigestible cartilage and tendons.

A sample of the variety of the remainder of our "menu" should be most informative. For breakfast, there was "black coffee," a tepid liquid whose color was all that resembled black coffee. For dinner, water soup was served: rutabagas, barley, or potatoes boiled in water. For supper, there was again black coffee (see above) and, occasionally, a roll. Potatoes (frozen in winter, mostly rotten in summer) and bread of poor quality and insufficient quantity were the mainstays of our diet, also food containing vast amounts of water and bulk. Most people responded to such a regime with gastrointestinal reactions, and/or agonizing polyuria which, naturally, would not be mitigated but aggravated by more generous rations.

Under such conditions, the fat (exclusively poor vegetable fat) and protein (hardly 10-percent animal protein) contents were obviously insufficient for the maintenance of health. As a consequence, the number of sick persons was staggering, with a mortality of one percent *per week* and more at certain times!

Occasionally, this generalized malnutrition resulted in peculiar ophthalmologic manifestations that I had never observed before.

In a series of cases I found evidence of typical and fully developed "crossing signs." Though Gunn was the first to observe this sign, I have described it as certain evidence of hypertension. Contrary to all previous experience, the blood pressure in this series was measured repeatedly and was found to be normal or even subnormal.

Almost all of these patients stated that they had suffered from hypertension for years, but that their old ailment had been cured by the "strict diet." All of them were in a deplorable condition. Those few that I could observe died of cachexia or some complicating illness within a few months.

I have described elsewhere this interesting exception for the importance of the crossing sign, nowaday a generally accepted sure sign of hypertension. May it suffice to say here that the heart muscle, weakened by malnutrition and protein deficiency, did not have the force to maintain the blood pressure at the required level. The changes in the retinal arteries, once developed, were irreversible.

Avitaminoses, another consequence of our diet, are of interest to ophthalmologists. The data previously enumerated indicated what the vitamin contents of our diet were like. The meat served so rarely at our "table" was practically free of fat. Margarine did not contain any vitamins whatsoever. Foods rich in vitamins, like fresh butter, milk, eggs, cheese, and fresh vegetables, were known to us only from hearsay. The American scientist, Casimir Funk, one of the pioneers in vitamin research, has pointed out that the danger of vitamin deficiency increases with malnutrition, whereas there is less need when there is an abundance of protein. Our camp, like all others, was bound to be host to a sample collection of all types of avitaminoses.

Hemeralopia, the earliest symptom of A-avitaminosis, spared hardly anybody in the camp. During my first months, I watched most people grope with outstretched arms, and yet collide frequently with one another, with trees, and other objects. The illumination was bright enough for me to recognize my surroundings quite well. There were frequent complaints of black and brown spots before the eyes, or of a black curtain descending at dusk. A few months later, I myself was in the same state and fumbled around in the evening. Now I, too, experienced all these symptoms. When I stepped from an illuminated room into a semidark street in the evening, I could not see the sky which was still light, or anything on the side. I walked as through a long, narrow, dark tunnel. Even today, my dark adaptation is distinctly retarted.

Xerosis of the conjunctiva and the well-known Bitôt spots were quite frequent. Usually associated with hemeralopia, they assumed an almost epidemic character early in the spring due to the activating influence of sun radiation. Xerosis was rare during the winter. According to numerous anatomic investigations, xerosis of the conjunctiva is, in short, a keratohyaline degeneration of the epithelium of the bulbar conjunctiva. Apparently, there is a secondary growth of xerosis bacilli. This growth forms the well-known, dry, whitish foam of the Bitôt spots that can be easily wiped off. The primary degeneration of the epithelium itself does not greatly change the gross appearance of the conjunctiva. Its luster is somewhat reduced, and the folds it forms when moved are rather coarse. These changes certainly are not marked enough to be of diagnostic significance.

Obviously, Bitôt spots develop in the presence of A-avitaminosis and degeneration of epithelium only after the invasion of xerosis bacilli. *Without xerosis bacilli, there can be no typical Bitôt spots.* Xerosis bacilli are harmless saprophytes that are frequently found in the normal conjunctiva. In my experience concerning the flora of the conjunctiva prior to cataract surgery, I estimate the frequency of this occurrence (either alone or together with other germs) to be between 25 and 30 percent. In only 25 or 30 percent of xerosis carriers may one be able to make a presumptive diagnosis of A-avitaminosis on the basis of the xerosis spots. In the remaining 70 to 75 percent, xerosis bacilli are missing and, except for hemeralopia, A-avitaminosis cannot be recognized on the basis of ophthalmologic findings. Of course, xerosis bacilli, not present

in the conjunctiva at first, may invade it later, thus causing an unpredictable drop in the 70 to 75 percent. This might explain the occasional occurrence of Bitôt spots in the epidemic proportions already mentioned.

In suspected cases, inoculation of the conjunctival sac with xerosis bacilli—either from a pure culture or traces scraped from a Bitôt spot—should cause the growth of a typical Bitôt vegetation on the degenerated epithelium that would serve as culture medium.

This simple means of inoculating the conjunctiva with xerosis bacilli could serve as a reliable yet innocuous test for A-avitaminosis in the absence of Bitôt spots and in the presence of doubtful hemeralopia. I have used this inoculation—even in my own eyes—in earlier experiments on various disinfectants for sterilization of the conjunctival sac before cataract surgery. As a rule, there was either no reaction or, only exceptionally, a slight conjunctivitis that lasted two or three days.

I was unable to carry out the experiments just outlined. The necessary equipment was not available. In addition, experiments involving bacteria were strictly prohibited (obviously, there was fear of bacteriologic warfare!). After I left the camp, cases with A-avitaminosis were not available for investigation.

No cases of keratomalacia in adults came to my attention. However, as already mentioned, some cases of keratitis that appeared quite harmless at first, suggesting the eczematous type, suddenly took such an exceptionally severe course that one could actually consider them as atypical cases of keratomalacia.

In children, xeroses of the conjunctiva and cornea were frequently observed, as well as true cases of keratomalacia. Frequently we had to treat other complications of A-avitaminosis, perhaps less serious but quite stubborn and annoying. I mention here the frequent occurrence of chalazia. Though not rare in everyday practice, they occurred in such numbers that a disturbance of the function of the meibomian glands due to avitaminosis had to be suspected.

Epiphora was quite frequent. In other instances, the lacrimal secretion was notably diminished.

The dryness and brittleness of the skin in cases of vitamin-A deficiency of long standing sometimes caused eye changes. In the tender, easily irritated skin at the canthi, especially the outer one, fissures and eczematous changes developed readily into the well-known angular keratoconjunctivitis. Frequently, the angles of the mouth showed similar changes.

Therapeutically, vitamin-A preparations proved to be successful along with local treatment. The course of many cases was quite protracted, and there were numerous recurrences. As a rule, supplementary treatment with vitamin-enriched food had to be omitted. Also, vitamin-A preparations could be used only most sparingly, especially for adults, because they were available in very limited quantities, and could sometimes not be obtained at all.

Evidence of B-avitaminosis with regard to the eyes was not really severe but quite frequent. In fact, it was surprising that it occurred at all, for our diet consisted principally of potatoes and bread and, therefore, should have contained vitamin B. Nevertheless, it seems that minimum requirements were not met. Probably, these requirements became greater in proportion as the fat content in our daily fare became smaller and the amount of carbohydrates was increased. Consequently our vitamin-B requirements became very high. What is more, the quality of our bread was inferior. The potatoes had been stored for a long time and were frequently spoiled, factors that were bound to cause further depletion of vitamin-B contents.

One sign of vitamin-B deficiency was a peculiar lid edema and a frequent chemosis of the bulbar conjunctiva in the absence of other causes. Usually there was involvement

of both eyes of varying intensity. Inflammatory conditions with ordinary more or less pronounced lid edema or chemosis, for example, hordeola, were of unusual severity and duration. Occasionally, one saw a retinal edema, with cloudiness and yellowish discoloration of the involved section. There was an occasional slight papilledema without other demonstrable etiologic factors. It is possible that frequent protean macular changes, such as I had seen only very rarely before, should be considered the result of B-avitaminosis. These changes consisted of white dots, occasionally with delicate star-like radiating patterns.

Typical cases of beriberi did not occur, as far as I know. Occasionally, though, there were cases of neuritis and other neurologic disturbances that were accompanied by edema and generalized weakness—a syndrome that, perhaps, represented a forme fruste of the disease.

Perhaps some cases of hunger edema (which were quite prevalent in the camp) should be considered here. For a while I myself had grotesquely swollen legs that did not cause particular discomfort and did not impair my work. After vitamin B_1 injections there was slow improvement.

True pellagra did not occur. Milder forms of the disease with symmetric changes and various nervous manifestations that could be called pellagroid were not rare.

Vitamin C was completely missing from our diet. In the absence of other etiologic factors, this might have been the cause of the rather frequent conjunctival and retinal hemorrhages.

If it is true that vitamin-C deficiency impairs the power to resist infections, the enormous number of recurrent abscesses, furuncles, styes, and so forth, could be considered as due to such a cause. However, poor hygienic conditions, like want of soap, crowded quarters, and insects, played their part.

Eye diseases as the result of D-avitaminosis were not observed. Cases of rickets in children did not occur in excessive numbers. Adults, mostly women, commonly showed signs of osteoporosis, the result of vitamin-D deficiency, that were manifested by dull pain in the region of the pelvis and the legs, by nervous states, by a tendency to fractures, and, particularly, by disturbances of motility.

Ocular changes caused by the deficiency of other known vitamins were not observed.

This brief review—principally seen from the standpoint of the ophthalmologist—cannot possibly give the essence of the life in such a camp. Only those who personally experienced the conditions from a medical point of view, from the point of view of administration of the camp, from the point of view of work distribution, who personally experienced the psychology of everyday life as well as some of the most outstanding events, will fully understand the significance of these camps. They were instruments of mass murder like gas chambers and machine guns, like the guillotines of the 18th century —only slower and not quite so efficient but more quiet and less conspicuous and, what is more, considerably cheaper.

Millions (among them a great number of physicians)—men, women, and children—lost their lives; 90 percent of all inmates died. If the Nazis had not run out of time in the last days of their debacle, the number would have been 100 percent.

Those few who escaped death by starvation, in gas chambers, or from machine guns, could not enjoy their regained lives. Many of them mourned the loss of their families, their wives, or husbands. All of them became beggars, worn out in body and soul. All of them were forced to start anew the struggle for their daily existence. The memory of terror and privation that was suffered for years, the memory of the horrible fate of so many relatives, friends, and comrades lingers on.

Via Andrea Doria 32.

A TOXIC OCULAR MANIFESTATION OF CHLORAMPHENICOL THERAPY

Report of a case of optic neuritis

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Two cases of optic neuritis caused by chloramphenicol (Chloromycetin) have been reported in the literature.[1,2] Permanent damage to the eyesight resulted in one case. Similar cases may have occurred but remain unreported or unrecognized because of milder symptoms. The serious potentialities in lasting damage to the eyesight demand that the possibility of optic neuritis be called to the attention of the medical man treating a patient with chloramphenicol. We therefore wish to add one more case to the two already reported.

Case report

N. L., aged 44 years, was given antibiotics for the treatment of subacute bacterial endocarditis over a period of nine and one-half months. The following is the course of treatment:

The patient was given 600,000 units of penicillin and 900,000 units of streptomycin daily for six weeks; then long-acting penicillin daily for two weeks. When he became allergic to penicillin, chloramphenicol was started. Two chloramphenicol capsules (250 mg. per capsule) were given every six hours (eight capsules per day) for seven weeks. Dosage was then reduced to six capsules per day for the next five months.

At the end of this period the patient was referred to us, complaining of blurred vision and a feeling of "looking through a film" for three

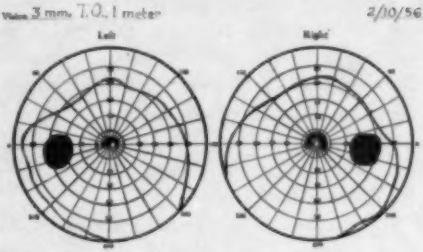

Fig. 1 (Cole, Cole, and Janoff). A pericentral scotoma was present in each eye.

weeks. His best corrected vision in each eye was 20/20 but he stated that the letters were not clear. The central field of the right eye was moderately constricted and slightly constricted in the left eye. Pericentral scotomas were present in both eyes (fig. 1).

Ophthalmoscopic examination revealed edema of the optic nervehead and dilation of the veins (fig. 2). The chloramphenicol therapy was suspended. The discontinuation of chloramphenicol was probably the most important factor in the complete recovery that was obtained in this patient but, in the interests of honest recording of all facts, thiamine chloride, vitamin B_{12}, and Diamox were used.

Two weeks later the patient stated that he could read and see more easily, but his vision was "not extremely sharp." He complained of numbness in the feet. The central field of the right eye was only slightly constricted and, in the left eye, it was

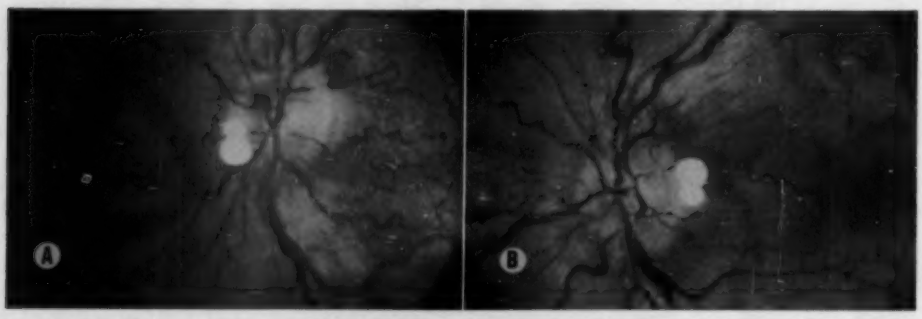

Fig. 2 (Cole, Cole, and Janoff). Edema of the optic nerveheads and dilation of the veins. (A) Fundus of the right eye. (B) Fundus of the left eye.

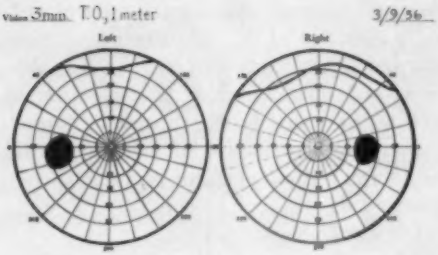

Fig. 3 (Cole, Cole, and Janoff). After treatment the pericentral scotomas had diminished in both eyes.

normal except for the pericentral scotoma which had diminished in both eyes (fig. 3). Diamox was continued and vitamin B_{12} and thiamine chloride were given weekly.

A month following the first eye examination and cessation of chloramphenicol, edema of the optic nerves had decreased and dilation of the veins was diminished. Visual fields were within normal limits and the scotoma was absent. Diamox was discontinued.

Discussion

The good name of a potent and useful drug is rapidly being tarnished by reports, such as this one, about its serious side effects. There is no question that chloramphenicol saves many lives. Rickettsial diseases, meningitis, bacterial endocarditis, and serious infections resistant to other antibiotics have responded to chloramphenicol. The severity of the side effects, therefore, does not justify condemnation of the drug. As with any drug, all possible side effects should be understood and anticipated so that treatment may be discontinued before irreversible damage is done.

The most frequently reported manifestations of chloramphenicol toxicity are aplastic anemias, anaphylactic reactions, skin eruptions, and mucous membrane irritations. Psychologic manifestations and paresthesias have also been noted. Optic neuritis, though apparently a rare result of toxicity, deserves a prominent place on the list of known toxic manifestations of chloramphenicol not only because of its serious nature but because of the implications. Since it is obvious that optic-nerve damage is a side effect of chloramphenicol, it might be useful to consider whether the psychologic effects noted may not be caused by similar damage to other structures of the central nervous system. The concentration of chloramphenicol in the cerebrospinal fluid is high, almost half that in the blood. Such a high concentration does not occur with other antibiotics of the tetracycline class.

In long-term treatment with any antibiotic or combination of antibiotics, frequent examination of the blood is standard practice. To this should be added *frequent examination of the fundus.* It is well to remember that the fundus is a useful diagnostic area. The possibility should be considered that the fundus may reveal the first signs of toxicity. Routine check throughout the course of chloramphenicol treatment in a number of cases should reveal whether this would be of value. At any rate, examination of the eyes by an ophthalmologist is mandatory if any other symptoms of toxicity, such as skin eruptions, appear.

On the basis of the two cases reported, and our case, the ocular symptoms of chloramphenicol toxicity are blurred vision, pericentral scotoma, and constriction of the visual field. Ophthalmoscopic examination in the case reported here revealed edema of the optic nerve and dilation of the veins. Lasky, Pincus, and Katlan[2] reported the same findings and, in addition, numerous hemorrhages in various parts of the fundus. Wallenstein and Snyder[1] found hyperemia of the optic nerve and disc margins obscured by edema of the nerve fibers.

Vitamin B_{12} appears to have corrected various conditions brought on by chloramphenicol toxicity. In our case, the optic neuritis was decreased after withdrawal of chloramphenicol and administration of Diamox, Vitamin B_{12}, and thiamine chloride. In the case reported by Lasky, Pincus, and Katlan, the condition was more advanced; while anemia and skin eruptions were cor-

rected, vision was permanently damaged. In their case no mention was made of vitamin B_{12}, only withdrawal of chloramphenicol.

Summary

A patient with an acute exacerbation of subacute bacterial endocarditis was given chloramphenicol daily for six and one-half months. During the last three weeks of this therapy, bilateral optic neuritis developed. With cessation of the chloramphenicol therapy and administration of vitamin B_{12}, Diamox, and thiamine chloride, the vision as well as the visual fields returned to normal.

Frequent examination of the eyes during long-term chloramphenicol therapy is recommended.

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GLAUCOMA DETECTION IN A GENERAL HOSPITAL*

A survey of 1,054 nearly consecutive admissions of patients over the age of 40 years

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Chronic open-angle (or chronic simple) glaucoma frequently produces no symptoms until it is quite advanced.[1] Chronic closed-angle (or chronic congestive) glaucoma may produce mild, transient symptoms, but occurs much less frequently than open-angle glaucoma.[1] Historically these two entities have the joint name of primary glaucoma[1] and it is only recently that we have learned to tell them apart.

It has long been recognized that advanced chronic open-angle glaucoma continues to get worse even though the intraocular pressure has been normalized by conservative and, when necessary, surgical treatment. Ophthalmologists are agreed, too, that, when discovered early, primary glaucoma responds more readily to treatment and has a far better prognosis.[2]

Primary glaucoma is unusual in the first two decades of life and only a few cases are seen in the third decade. It is in persons in the middle forties that the number of cases begins to increase, reaching a peak in the fifth and sixth decades.[3] Finger tensions are of practically no value in detecting early cases of chronic primary glaucoma. Leaders in the field have strongly urged that ophthalmologists do tonometry on all their patients over 40 years of age.[4] Some advocate routine tonometer tensions from the age of 35 years.[5]

Primary glaucoma is prevalent in all countries and has no racial preference.[3] In the first three decades of this century it accounted for from one to two percent of ophthalmic cases.[3] Lehrfeld and Reber[6] reported 1,876 cases of primary glaucoma in 242,533 patients entering Wills Hospital from 1926 to 1935, an incidence of 0.78 per-

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* From the Ophthalmology Section, Ann Arbor Veterans Administration Hospital, and the Department of Ophthalmology, University of Michigan Medical School. Read at the Sixth Triennial University of Michigan Medical Alumni Conference, Ann Arbor, September 28, 1956.

cent; 784 of the 1,876 glaucoma patients, or 42 percent, already had vision less than 20/200 when coming to the hospital. Such cases are discouraging to treat. Schoenberg, in 1945, in outlining steps to control glaucoma, pointed out that, in the United States, there were 20,000 persons blind from it in both eyes and 150,000 in one eye.[7]

We knew nothing of the incidence of chronic primary glaucoma in the general population until 1951 when Brav and Kirber reported a mass survey of workers, aged 40 to 65 years, in Philadelphia.[2] They discovered 153 definite or early cases of chronic simple glaucoma in 10,000 persons, or 1.53 percent.

On one day in Cleveland in 1953, 12,803 persons had tonometer tensions, and Wolpaw and Sherman reported a 1.87 percent incidence of chronic glaucoma.[8] They emphatically stated, however, that a short mass survey was *not* the best way to detect early glaucoma, but that a continuous effort should be made. Certainly a mass survey should not be done unless each suspect can obtain a complete ophthalmologic examination and adequate follow-up.

Gundersen[5] in 1954 emphasized that, of the two most common forms of preventable blindness, glaucoma and amblyopia ex anopsia, chronic open-angle glaucoma is the most important. He also urged that physicians and medical students be taught to do tonometry.

Zeller and Christensen[9] in Oregon in 1954 taught interns to do tonometry, and 60 patients in 1,000 over 40 years of age were found to have tensions above 25 mm. Hg. Positive serologies for syphilis in Oregon then were 17 percent of 100,000 in those patients over 40 years of age compared to an estimated 2,000 cases of undetected glaucoma per 100,000 in those over 40 years of age. Yet no intern did another tonometry after leaving their service. They logically concluded that tonometry should be taught to medical students. The teaching of tonometry to medical students has recently been begun at the University of Michigan. In 1955, Vaughan and co-workers[10] found a 1.9 percent incidence of glaucoma in 1,000 persons in a California mental hospital.

Glaucoma surveys thus serve to detect early cases of chronic primary glaucoma and to demonstrate that it is more prevalent than has been suspected.

Procedure

The Ann Arbor Veterans Administration Hospital is a general medical and surgical hospital co-operating with the University of Michigan. From October 31, 1955, to June 4, 1956, there were 2,144 patients admitted; 1,114 of these were aged 40 years or over. Intraocular pressures were taken on the wards with standard Schiøtz tonometers, usually with a 7.5-gm. weight. Anesthesia was with 0.5-percent tetracaine (Pontocaine) hydrochloride. Between tests the footplates were cleaned with carbon tetrachloride or wiped free of a 1:5,000 aqueous Zepharin solution in which they stood. No overt conjunctivitis, keratitis, or other complication resulted.

Results

Of the 1,114 patients aged 40 years or over, intraocular pressure was done on 1,054. The discrepancy of 67 patients is accounted for as follows: 37 were readmissions with previously normal tensions and 30 had none taken. The 30 with no tensions taken were broken down as follows: 11 died shortly after admission, five left the hospital within 48 hours of admission, seven were uncooperative or on strict isolation, and seven were discharged without tensions being taken.

Of the 1,054 patients who had tonometry, there were 10 known cases of glaucoma and 55 new suspects with tensions over 25 mm. Hg (1948 accepted scale[11]). Thirty of the 55 suspects had tensions of 26 mm. Hg (23.5 mm. new 1954 scale[12]) in one or both eyes; the other 25 had higher tensions. Of the latter 25 all were studied except one who

died. Of the 30 with tensions of 26 mm. Hg, 24 were studied, three died, and three had no follow-up. Thus 47 of the 55 suspects were studied. Twenty-two of the 47 suspects appeared normal on repeated tonometries alone. The remaining were studied further. Diagnoses were made by history, examination, repeated tonometer tests, visual field studies, water-drinking tests, dilated tensions, and gonioscopy with the Allen-Thorpe gonioprism.[1,13]

There were 18 cases of glaucoma among these 1,054 patients or 1.71 percent. Of these 18 cases, 10 were previously known and eight were new. The 10 known cases were three of chronic open-angle glaucoma, two of secondary, one of acute closed-angle, and four of absolute glaucoma from old injury. The eight new cases were of chronic primary glaucoma, seven of chronic open-angle, and one of chronic closed-angle. None of these eight cases had yet lost central visual acuity, though two already had field changes near the fixation point. Two of the eight cases (open-angle) had a definite family history of glaucoma.

Besides the eight definite cases, one suspicious case continues to be observed. The seven open-angle cases have been controlled by miotic therapy and the closed-angle case with peripheral iridectomies.[14] Two of the eight cases had initial tensions of only 26 mm. Hg. All but two of the eight cases already had field changes in one or both eyes; the two who did not have field changes had positive water-drinking tests and tensions over 32 mm. Hg.[1]

Discussion

Our finding of 55 new suspects among 1,054 hospital admissions compares reasonably with Zeller and Christensen's[9] finding of 60 suspects among 1,000 hospital patients (5.2 percent versus 6.0 percent). The eight new cases of chronic primary glaucoma detected among 1,054 nearly consecutive hospital admissions (aged 40 years and over) produce a standard error of plus or minus 0.3 percent. In other words, doing repeated surveys in the same place on the same sort of persons would reveal from five to 11 new cases of chronic primary glaucoma two thirds of the time in the same number of hospital admissions.[15] This is a lower incidence[2] than Brav and Kirber's finding of 1.53 percent, but falls within Kronfeld's[16] recent estimate of one to two percent undetected cases of primary glaucoma in the United States in persons over the age of 40 years.

It would seem that 1,054 almost consecutive admissions to a general hospital are more like a sample of the population than, for example, 1,000 patients in a mental hospital, but still are not comparable. To illustrate: the ages of the persons surveyed were as follows: 40-49, 272 or 27 percent; 50-59, 241 or 23 percent; 60-69, 435 or 41 percent; 70-79, 71 or 6.0 percent; 80-89, 24 or 2.0 percent; and 90 and over, none. In Michigan in 1950 only 20 percent of the population was in the 60-69 age group. As 41 percent of surveyed patients were in the 60-69 age group, our study probably has a higher percentage of older persons than found in the general population, a factor that might tend to make our incidence of glaucoma higher.

Why is our incidence lower than that in the few existing studies?

Sixty-two of our 1,054 patients were Negroes, five were white women, and the rest were white men. Though race does not influence the incidence of primary glaucoma, sex is believed to at the rate of about six to five women over men.[3] With all but five of our 1,054 patients being men, our incidence may have been lowered by this factor.

Another factor that might have lowered our incidence is the difference in locality. Our patients came chiefly from Michigan outside of Detroit. They did not live in a huge metropolitan area like Philadelphia. Stress has long been recognized as having more than an incidental relationship to closed-angle glaucoma, and some ophthalmologists feel it plays an etiologic part in

chronic simple glaucoma.[20, 21] In recent years we have come to believe that huge cities are more productive of human stress than more sparsely settled areas.

Chronic open-angle glaucoma may be dominantly inherited.[17] Two of seven cases of chronic simple glaucoma detected in this survey had a positive family history of glaucoma. Relatives of patients with chronic open-angle glaucoma are a fertile field for the detection of early cases and Fralick has recommended that these relatives of known cases have periodic glaucoma work-ups after the age of 40 years.[18, 19]

Based on the 1950 U. S. census we might guess that there are 371,544 patients, aged 40 years or over, with undetected chronic primary glaucoma in the United States aged 40 years and over. As both the population and the relative number of those aged over 40 years is increasing, we must certainly continue our efforts to discover these patients early and get them under competent ophthalmologic care before they are visually incapacitated.

SUMMARY

A survey of 1,054 nearly consecutive admissions to a general hospital in Michigan revealed an 0.76-percent incidence of previously unknown cases of chronic primary glaucoma. Seven of these cases were chronic open-angle glaucoma and one was chronic closed-angle glaucoma.

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EARLY DIAGNOSIS OF PRIMARY GLAUCOMA*

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Recent glaucoma studies have made no more important clinical contribution than making possible earlier diagnosis of glaucoma with increasing frequency. Few things about glaucoma are more generally accepted than that therapy undertaken before much structural damage occurs in the eye is more effective. The terminology and concepts of closed-angle and simple primary glaucoma are now internationally accepted, despite debate and some disagreement about the true nature of these major divisions of primary glaucoma. It is therefore important not only to diagnose but also to classify primary glaucoma according to these concepts, since closed-angle glaucoma offers therapeutic opportunities not present in comparable degree in simple glaucoma.

SCREENING TECHNIQUES FOR CASE FINDING

If very early glaucoma is to be found, it must be looked for assiduously. The following represents an effective minimum screening routine for glaucoma:

1. HISTORY

The importance of leads gained from a carefully taken history cannot be overestimated. A familial background of glaucoma should be inquired into, since a genetic determination of many cases is well known. Such symptoms as transient blurring of vision, associated headaches, feeling of pressure about the eyes, and observation of haloes about lights, all should be regarded as suspicious. Frequent changes in the refractive status, without visible lens change or a metabolic explanation, should also be regarded with suspicion.

2. ANATOMIC CHANGES

Any cupping of the disc suggestive of glaucomatous cupping should be regarded with suspicion, since all glaucomatous atrophy has to have a starting point and since glaucomatous cupping cannot be accurately differentiated from that which is nonglaucomatous by a single visual examination. Very shallow anterior chambers and narrow chamber angles should be considered dangerous, especially when there are symptoms in any way suggestive of mild congestive attacks.

3. ROUTINE TONOMETRY AND VISUAL FIELD TESTING

Tonometry should be done routinely on all patients aged 35 years and over and on any younger ones in whom there is any suggestive history or physical findings. With the availability of the Harrington[1] multiple pattern, tachystoscopic field screener, it is now feasible to screen the visual fields of all individuals in this same age group, plus suspicious younger individuals.

Whenever the intraocular pressure is 23 mm. Hg (Schiøtz) (1954 scale) or above, or when there is a difference between the two eyes of more than 5.0 mm. Hg; whenever there is any field change on the tachystoscopic screener; or whenever anything in the history or physical examination suggests glaucoma, further detailed study should be made to rule glaucoma in or out within the limits of our present knowledge.

TECHNIQUES FOR DEFINITIVE DIAGNOSIS OF EARLY GLAUCOMA

It should be recognized that it is often or even usually not possible to make a definite diagnosis, or particularly exclusion, of glaucoma by a single examination. In many cases it is only after follow-up examinations over

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a period of months, or even years, that the diagnosis of glaucoma can be made, or particularly excluded, beyond any question. However, there are certain techniques of testing which should be employed, with variations according to clinical judgment of the individual case, and which must be done repeatedly if an accurate evaluation of the case and its progress is to be obtained. These include field testing, intraocular pressure and aqueous outflow studies, provocative testing, gonioscopy, and systematic follow-up of anatomic changes, particularly in the optic disc.

1. Visual field testing

The ideal technique for visual field testing must be simple for the inattentive observer to perform and readily reproducible by various operators. Certainly the ideal method has not yet been found. The Glaucoma Symposium organized by the Council for International Organizations of Medical Sciences in 1954 suggested that the field taken on the tangent screen with the 2/1,000 white test object is satisfactory and this is certainly a wise choice when the patient is an inaccurate observer or if the visual acuity is at all subnormal.

Most patients of average intelligence are, however, quite able to learn to perform an accurate field with a 1/1,000 white test object. Certainly the added sensitivity of the 1/1,000 white isopter will pick up defects which will be missed completely with the 2/1,000 white test object. In my hands the use of fluorescent test objects with black-light illumination, as suggested by Harrington,[2] has been a great help with the 1/1,000 and the 0.5/1,000 white isopters, making possible far greater reproducibility of fields at this level, as well as giving maximum freedom from outside distractions when these fields are done in a quiet room, darkened except for the black light.

The use of such illumination with a pantoscopic tangent screen and magnetic test objects, such as that described by Gunkel and Ryan,[3] seems a long step toward an ideal form of central field testing.

The 2/1,000 white test object may be put to excellent use for teaching patients the technique of central field testing, and also for determining whether or not field loss is progressing definitely enough to demand a change in therapy when the diagnosis has been well established.

In testing the visual fields, careful attention should be given to proper head positioning, to significant refractive errors which affect visual acuity, and to avoidance of extreme miosis, fatigue, or the effect of cataracts, all of which may produce false field defects.

Usually, the earliest field defects which may be detected include various types of enlargement of the angioscotomas (Seidel defects, asymmetric enlargement of the blindspot, the Bjerrum defects) plus more advanced defects, such as superior field depression, step defects, and baring of the blindspots. All of these defects must be regarded as pointing toward glaucoma, especially when they may be reproduced on repeated tests. However, they are by no means diagnostic when found only on a single examination which cannot be reproduced later.

Flicker fusion fields are occasionally helpful but in my hands these have been disappointingly inconsistent and have shown rather poor correlation with fields taken by more standard techniques. The multiple pattern tachystoscopic visual field tester appears to be not only a very excellent quick method of picking up the presence of defects for screening but also for working with patients who are inaccurate with the usual field techniques, or are sick or easily distracted. In my hands its sensitivity would appear to approximate the field with the 2/1,000 white test object.

2. Intraocular pressure and aqueous outflow testing

Intraocular pressure should be tested, using both the 5.5-gm. weight and 10-gm.

weight on the tonometer to evaluate the scleral rigidity. Several such paired readings should be taken to obtain a useful estimate of scleral rigidity; small differences between the values obtained with the two weights are not clinically important. High scleral rigidity will make the reading with the 5.5-gm. weight higher than the actual pressure in the eye, but lower than the reading with the 10-gm. weight. Friedenwald's[4] scale can be used with these two measurements to estimate the scleral rigidity.

The importance of phasic variation in the tension cannot be overemphasized. The normal diurnal swing of tension should fall within a range of 5.0 mm. Hg or less, and the earliest evidence of simple glaucoma may be an abnormal variation of the diurnal curve. This may be checked roughly by having the patient return to the office at as wide a spread of time as is feasible during working hours but a 48-hour tension curve should be done in suspected cases which cannot be clearly confirmed otherwise. Whenever possible tonography should be done repeatedly during the course of taking this tension curve.

Tonography now seems essential for thorough and accurate glaucoma work and particularly when early diagnosis of glaucoma is attempted. However, if the technique is to be of any great value it must be performed under carefully controlled conditions and with meticulous attention to details.

A recording device, in addition to the electronic tonometer, is most helpful in disclosing poor readings, bad functioning of the electronic tonometer and/or of the patient and operator, and also in making possible easier and better estimates of the C value (facility of aqueous outflow) from graphic charts.

Accurate calibration and a high sensitivity of the instrument set-up is necessary for good tonographic studies, and variation in the instruments make a calibration micrometer of great help in checking the accuracy of the instrument, as well as in making calibration scales for the tonograms.

A constant voltage transformer often does more harm than good and can be dispensed with except in very unusual conditions of circuit overloading, which ordinarily are readily disclosed by the tracing with a recording device.

The cylinder and plunger of the electronic tonometer should be cleaned after each use in order to avoid sticking from mucus or other foreign material.

The effect of tonography on the intraocular pressure in the opposite eye, through a central mechanism not clearly understood, should be recognized, and an initial tension determination should be made before tonography, unless there is to be a considerable time interval between tonography on the two eyes.

Good anesthesia, an easy and comfortable fixation device, clear explanation of the test to the patient, delicate handling of the lids and placing of the tonometer on the cornea, loosening of any pressure or constriction about the neck, and avoidance of distracting influences in the room during tonography, are all of great importance in getting accurate results.

While there are valid defects in Grant's[5] formulas and charts, these are essentially suitable for clinical use. We know that C values for a given eye are usually fairly constant within the limits of phasic variations, but values down to 0.11 may occasionally be seen in otherwise normal eyes. However, values below 0.15, using Grant's charts, should certainly be considered suspicious and, if constantly below this level on repeated checks, certainly must be considered significant. The exceptions to this include eyes with low initial tensions (initial scale reading 5.5 mm. Hg or below) where fairly low C values are rather frequent in normal eyes, and also in some cases with extremely abnormal scleral rigidity. Ballintine's mono-

graph on *Clinical Tonography*[6] is an excellent source of charts and data useful in tonography.

Tonography is not only useful in diagnosing simple glaucoma but also in helping to classify equivocal cases. Since it is well known that simple glaucoma can occur even in the presence of very narrow chamber angles, gonioscopic classification alone is often impossible. However, if the facility of outflow is low, with an open angle and normal or near normal tension, closed-angle glaucoma can be excluded at that time; if it is high with a partly closed or very tight chamber angle, even when the tension is slightly above normal levels, an angle-closure mechanism is a likely consideration.

3. Provocative testing

While it should be repeatedly emphasized that no negative provocative test excludes glaucoma, these tests have great value, chiefly in three areas:

1. In confirming, when positive, suspected diagnosis of glaucoma.

2. In aiding with the classification of primary glaucoma.

3. In determining the margin of safety of a therapeutic course, especially in closed-angle glaucoma.

While the diagnosis is usually easy in cases of acute congestive closed-angle glaucoma, it appears that closed-angle glaucoma may often be diagnosed in a prodromal or preglaucomatous phase, or when it is a subacute disease, before acute congestive attacks occur. These cases often show symptoms suggesting mild congestive episodes, such as headache associated with haloes and transient blurring of vision, and may be found to have occasional high normal or low abnormal intraocular pressure levels, with chamber angles of quite narrow contour but only partly, if at all, closed.

In these cases, dark-room provocative tests may often clinch the diagnosis and demonstrate how truly dangerous the potential eye condition is. When positive, these tests may disclose not only a rise in the intraocular pressure but also a fall in the C values. In these cases it may also be possible to demonstrate angle closure gonioscopically, especially if care is used with the illumination for gonioscopy to avoid opening the angle by miosis from the strong light before the angle closure can be observed.

When dark-room provocative tests are negative, mild mydriatics (preferably *not* sympatheticomimetic) may be used safely under close observation and may give many additional positive results.

Although a negative result from both these tests by no means completely excludes the diagnosis of closed-angle glaucoma, it makes possible a feeling of considerable security from the danger of acute congestive episodes in patients left untreated.

When simple glaucoma is suspected, the water-drinking test may be most helpful. In the positive response, the tension alone may rise more than 6.0 to 7.0 mm. Hg (Schiøtz), often without tonographic evidence of a lowered facility of aqueous outflow, since the rise here appears to be chiefly a result of increased formation of aqueous with poor adaptation of the outflow channels in the glaucomatous eye to the increased load. The chamber angle, of course, remains open gonioscopically during the rise in tension. There may, however, be a fall in the facility of outflow, even when the pressure rise is equivocal, and thus tonography may add to the usefulness of this provocative test. Becker[7] has recently pointed out the diagnostic significance of the ratio between the initial tension and facility of aqueous outflow after the water-drinking test, particularly when Friedenwald's latest calculations are used to obtain those values.

The Priscoline test, performed by subconjunctival injection of 0.01 gm. in one cc. of physiologic saline, appears to be the other provocative test of greatest value in

simple glaucoma. To be considered positive, it must produce a rise in the tension of 10 mm. Hg (Schiøtz) or more. It also does not significantly change the facility of aqueous outflow in most cases and, of course, it does not affect the angle contour. Its chief disadvantage is the need to perform an often painful injection beneath the conjunctiva.

It should be emphasized that all therapy should be stopped at least 24 to 48 hours before provocative testing if the test is to have a fair chance. Since the tests are relatively specific for the types of glaucoma in which they may give positive results, their helpfulness in classifying, as well as diagnosing, borderline cases is obvious. In closed-angle glaucoma, positive pupillary dilatation tests emphasize the need for active therapy.

4. Gonioscopy

The study of the anterior chamber angle is of critical importance in the accurate classification of glaucoma. While it should be remembered that simple glaucoma may occur with any type of angle contour and with no really characteristic chamber angle findings at all, in closed-angle glaucoma the tension rises only with complete or partial angle closure.

Repeated or long-continued episodes of angle closure usually lead to the formation of anterior peripheral synechias, with adherence of the iris to, or anterior to, the trabecula. The glaucomatous anterior peripheral synechias must be clearly differentiated from strands of iris tissue, or pectinate ligamentlike remnants, bridging the ciliary body or even extending up to the trabecula and Schwalbe's line. It is probable that in occasional cases an angle-closure episode may occur in simple glaucoma, when the chamber angle is quite narrow, giving in effect both simple and closed-angle glaucoma in the same individual.

The light used for gonioscopy may open the closed chamber angle by its miotic effect, thus obscuring the angle closure from the observer. This possibility must be lessened by having the microscope in observing position before the light is actually thrown on the chamber angle.

With all the testing techniques, it is often impossible to diagnose beyond any question early glaucoma in one or two visits, and even more impossible to exclude it beyond doubt. In such cases, long-term follow-up examinations may be necessary to make a definite diagnosis, with attention to the intraocular pressure, facility of aqueous outflow, visual field changes, and anatomic changes. The use of photography to follow changes accurately, particularly in the optic nervehead but also in the chamber angle, is invaluable. When such photography is not available, systematic drawings, especially of the disc, are most helpful. Certainly early glaucoma cannot be found except by persistent and careful search, and I am sure that its detection is in direct proportion to the diligence with which it is sought.

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THE EYE IN OLD AGE*

IV. Ocular survey of over one thousand aged persons with special reference to normal and disturbed visual function

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In 1952, a survey of the ocular status of 1,000 aged persons was undertaken to determine how many were handicapped visually and to study the causes of such disability. Statistical studies in the past have dealt chiefly with the incidence and causes of blindness (Sorsby[1] in England, Holst[2] in Norway, Lancaster and Foote[3] in the United States, Sveinson[4] in Iceland, and, more recently, Bjornsson[5] in Iceland).

Other statistical studies have dealt with the frequency of cataract or glaucoma and their relationship to age. Of special interest was the work of Fischer and Gjessing[6] which purported to show that the curve of incidence of cataract is an S-shaped curve of saturation, indicating that the expectancy of cataract is almost 100 percent, if the individual lives long enough. Other studies such as those of Horlacher,[7] Barth,[8] Anderson,[9] Gradle,[10] and Samuels and Fuchs[11] also showed a similar tendency.

In glaucoma, an increasing percentage of cases with increasing age was noted by Priestly-Smith[12] in England, Schmidt-Rimpler[13] in Europe, Lehrfeld and Reber[14] in America, Bell[15] in hereditary studies, Haag,[16] Carvill,[17] Pillat[18] and in Bjornsson's study of blindness in Iceland,[5] especially in people over 60 years of age.

Other authors have described the changes in the individual ocular tissues attributed to old age and the aging process. Among these may be mentioned the works of Salzman,[19] Wilmer,[20] Terrien,[21] Vogt,[22] Crisp,[23] Rones,[24] Berens,[25] and Fischer.[6] But a study such as this one which attempts to cover all ocular disabilities in a single large group of individuals, and attempts to correlate both ocular and medical changes, has not been done before to our knowledge.

The facilities for this work were available at The Home for Aged and Infirm Hebrews of New York City. Here, complete records are kept of the residents who are under continuous observation from the time of admittance until they die. They are a homogeneous group of old Jewish men and women who have sought institutional care for a variety of reasons, chiefly physical disability. Economic and social factors have also played a part. The total population may be classified as to functional capacity as follows:

		Percent
A	Ambulatory (completely self-sufficient)	18
B	Ambulatory (moderately handicapped)	33
C	Semi-ambulatory (needing nursing care)	26
D	Bedbound (or sharply limited in activity, needing nursing and medical care)	23

The ages in our series ranged from 65 years to over 90 years, with most of them in the 70-to-80-year decade, and the next largest group in the 80-to-90-year decade. A small but significant number are over 90 years of age. The general medical status is recorded on admission and at yearly check-ups. Appropriate laboratory studies are made in each case.

Complete eye examinations are done and repeated yearly. In this connection it is necessary to state that poor vision is not a bar to admission to the institution, as long as the individual can see well enough to get

* From the Medical Service, The Home for Aged and Infirm Hebrews of New York. This work was supported by a grant from the U. S. Department of Health, Education, and Welfare, National Institute of Neurological Diseases and Blindness (B-154). This paper was read before the New York Society for Clinical Ophthalmology on October 3, 1955.

around and take care of himself. Occasionally even a totally blind person may be admitted.

Finally, at death, it has been possible in a goodly number to obtain post-mortem examinations of viscera, brain, and eyes. In this manner, a great fund of information has been accumulated and correlated. Some of these findings have been reported before by the authors individually and collectively.[26-29, 37]

In this report the findings of the ocular survey will be emphasized statistically as to age and sex and associated conditions. Visual acuity as the prime expression of ocular function will be discussed at first, followed by figures indicating the frequency of occurrence of cataract, glaucoma, and diseases of the macula, since these conditions are the ones most frequently responsible for loss of visual acuity. Subsequent studies aim to bring out possible correlations between significant eye conditions and disorders in other parts of the body, that is, arteriosclerosis, heart conditions, diabetes, and mental disorders.

The visual acuity (table 1) was determined by retinoscopy and refraction. The total number of residents examined over a three-year period was 1,068 persons, of whom 398 were males and 670 were females. The preponderance of females (60 percent) to males (40 percent) is fairly typical of this aged population though percentages vary in different vital statistics studies.[20, 21]

Table 1 is a complete record of the visual acuity of each eye of the entire group, as found on the Snellen chart, and subdivided according to the age decade and sex. The total figures for each decade are listed. The findings for the total 2,136 eyes may be summarized as follows:

Vision	Degree	Eyes	Percent
Good to useful	15/15 to 15/40	1,523	71.4
Fair to adequate	15/50 to 15/70	315	14.7
Poor	15/100 to 15/200	125	5.8
Very poor	15/300 to light perception	141	6.6
No light perception		32	1.5

If the first and second groups are combined, good to adequate vision is present in 86.1 percent of the entire number of eyes; poor vision to no light perception was present in 13.9 percent.

The figures were studied further to determine whether they varied in any way in the different age decades. The number of eyes in the 60 to 70 group is too small statistically because it is only a small sample of the number of people in this age group in the total population, since many individuals in this age group do not seek institutional admission. This objection does not hold, however, for the over 90 years of age group, since here the tendency is for such aged individuals to be in a home, and they therefore

TABLE 1

VISUAL ACUITY

Age Group (yr.)	Good to Useful Vision										Fair to Adequate				Poor				Very poor		No Light Perception		Total
	15/15		15/20		15/25		15/30		15/40		15/50		15/70		15/100		15/200		15/300		No L.P.		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	
60 to 69	11	15	32	55	12	29	12	34	9	19	3	7	1	5	0	0	4	3	3	8	1	4	267
70 to 79	6	7	100	143	66	124	73	182	44	114	20	44	14	44	4	12	6	23	18	37	4	13	1,098
80 to 89	1	9	39	41	32	46	74	71	50	64	35	55	25	49	10	16	20	19	29	40	6	3	725
90 and over	0	0	2	1	0	2	1	7	3	2	5	5	1	2	3	2	1	2	3	1	1	0	46
Total	18	22	173	240	110	201	160	294	106	199	63	111	41	100	17	30	31	47	55	86	12	20	2,136

TABLE 2

VARIATION OF VISUAL ACUITY IN SUCCEEDING AGE DECADES

Visual Estimate	Age (yr.)							
	60–69		70–79		80–90		90 and over	
	No.	%	No.	%	No.	%	No.	%
1. Good	228	81.64	859	78.23	418	56.5	18	39.2
2. Fair	16	5.99	122	11.11	164	23.1	13	28.2
3. Poor	7	2.62	45	4.08	65	9.4	8	17.4
4. Very poor	11	4.12	55	5.01	69	9.7	6	13.1
5. No light perc.	5	1.8	17	1.55	9	1.3	1	2.1
Totals	267 eyes		1,098 eyes		725 eyes		46 eyes	

represent a large percentage of the entire population of this age group. Table 2 shows the results of this study.

These figures are graphically represented in Chart 1. Thus, it can be readily seen that good to useful vision declines in each succeeding decade but fair to adequate vision increases in percentage as the person ages. Poor and very poor vision also increase perceptibly in the older age groups.

For the sake of further simplification, the figures may be compared in two large groups —those under 80 years of age and those over 80 years of age. The vision may also be divided into two groups: (1) good to adequate vision; and (2) poor vision to no light perception. Table 3 shows these figures. This result is graphically represented in Chart 2. Good to adequate vision diminishes about 10 percent in the older age group over 80 years, while poor vision increases to a similar degree.

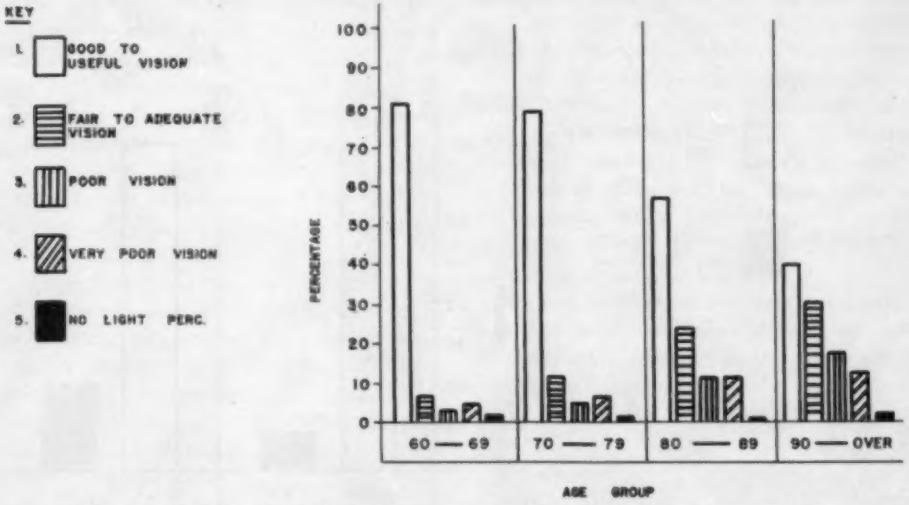

Chart 1 (Kornzweig, Feldstein, and Schneider). Percentage variation of visual acuity in succeeding age decades.

TABLE 3

VARIATION IN VISUAL ACUITY UNDER AND OVER 80 YEARS OF AGE

	Under 80		Over 80	
	No.	%	No.	%
Good to adequate vision	1,245	91.2	613	79.6
Poor vision to no light perception	120	8.8	158	20.4
Totals	1,365		771	

CATARACT

Cataract formation is definitely one of the concomitants of old age. All statistics so far have shown that it is inevitable if one lives long enough.[6–11] However, when the figures are examined from the point of view of visual function, it is surprising how relatively few individuals are sufficiently handicapped visually to require surgical correction. It was with this view in mind that our figures were compiled. It was felt that little that is new would be gained by listing all the different clinical varieties of cataract in the aged.

According to the standard nomenclature, there are only two groups of cataract in the aged, (1) diabetic and (2) senile. Under the latter are listed all the different types of senile cataract: (a) black cataract, (b) sclerosed lens, (c) hypermature cataract, (d) incipient cataract, (e) lamellar separation of lens, (f) mature cataract, (g) morgagnian cataract, (h) nuclear cataract, (i) peripheral wedge-shaped opacities, and (j) water fissure in lens.

For our purpose, the residents with cataract were listed under the following four groups. The classification into these groups is based on visual function rather than structural changes in the lens:

CATARACT	VISION
1. Incipient—	Up to 15/30
2. Immature—	From 15/40 to 15/70
3. Operable—	From 15/100 or less
4. Operated	

In these cases the vision was reduced solely by the cataractous changes and there was no associated glaucoma or macular disease. In patients with operable cataracts where the fundus could not be seen, it was assumed that the visual impairment was due to the cataract unless the examination or history indicated otherwise.

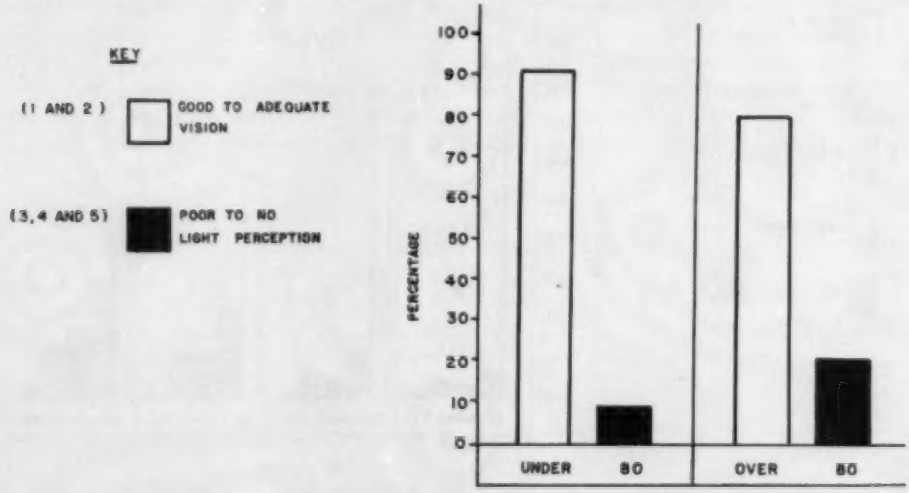

Chart 2 (Kornzweig, Feldstein, and Schneider). Percentage variation in visual acuity under and over 80 years of age.

TABLE 4

PERCENTAGE AND VARIETY OF CATARACT IN THE UNDER AND OVER 80 AGE GROUPS

	Incipient Cataract			Immature Cataract			Operable			Operated			
	M	F	%	M	F	%	M	F	%	M	F	%	Total
Under 80	112	182	41.2	86	246	46.5	18	31	6.9	8	30	5.4	713
Over 80	61	59	20.4	127	211	57.6	35	37	12.2	26	31	9.8	587
Total	173	241		213	457		53	68		34	61		
Grand total	414			670			121			95			1,300

Table 4 shows the number of cataracts of all types divided according to the above classification, and further subdivided according to age and sex. The age was listed as either below or above 80 years—since most of the patients are in these two decades.

The total number of eyes with cataracts of all types was 1,300 or 61 percent of the entire group. Of the under 80 group, 713 eyes had cataract or 52.1 percent of all eyes in this age group. In the older age group over 80, 587 eyes had cataract, or 76 percent of all eyes in this age group. This is in agreement with other observers who recorded the increasing incidence of cataract as the individual grew older. It will be noted, however, that only 121 eyes were in the operable group and only 95 eyes were operated upon. The operable eyes—121—represent 9.3 percent of all cataract eyes and 5.6 percent of the entire group. Those eyes actually operated for cataract—95—represent 7.3 percent of all cataract eyes, and only 4.4 percent of the total group.

These figures warrant an explanation. Of all the eyes in over 1,000 aged persons, 2,136 in number, only 95, or 4.4 percent, were actually operated upon for cataract. There are several reasons for this. Many older people have one eye that is stronger than the other, and operation is delayed until the better of the two eyes begins to fail. Also, many older individuals are contented with their limited vision in their limited sphere of activity. Others may be too infirm for surgical intervention, though lately this group is growing smaller due to increasing awareness of operative possibilities.

A graphic presentation of the percentage of the different types of cataract in the two large age groups is shown in Chart 3. The incipient group decreases, but all other groups, immature, operable, and operated groups, increase in the older age section.

OCULAR TENSION AND GLAUCOMA

In a survey such as this, certain fixed standards have to be set as to what constitutes normal and abnormal intraocular pressure. It is generally agreed that tension up to 25 mm. Hg as estimated on the Schiøtz tonometer is normal tension. Tension over 30 mm. Hg is also generally agreed upon as being abnormally elevated tension and indicates a glaucomatous state. Tension between 25 and 30 mm. Hg is considered possibly or potentially glaucomatous. These limits of intraocular pressure have been used by us as a basis of classification in our study of intraocular pressure in old age.

At the completion of the survey, the intraocular pressure was taken at least once on 1,897 eyes. On many of these eyes this test was repeated several times.

The figures for the entire group are as follows:

TENSION (mm. Hg)	EYES	PERCENT
Up to 25	1,604	84.5
26 to 30	194	10.2
31 and over	99	5.3

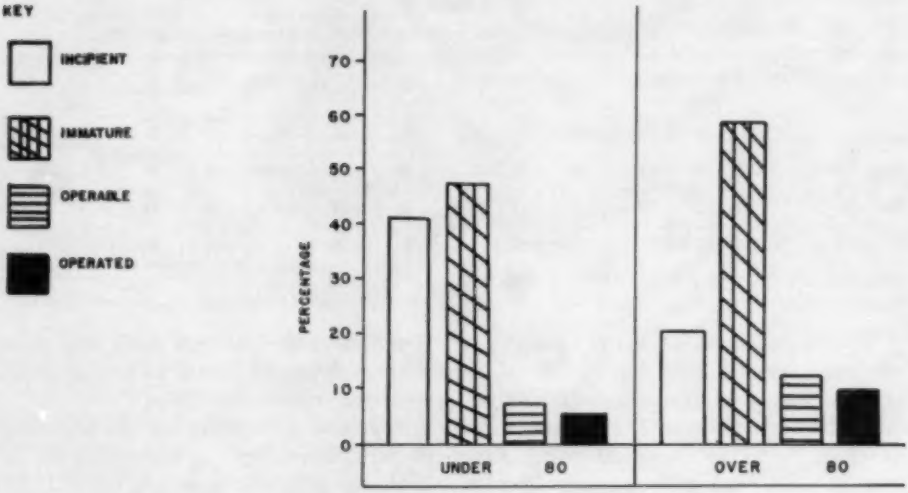

Chart 3 (Kornzweig, Feldstein, and Schneider). Percentage variation of the varieties of cataract in the under and over 80 years age groups.

These figures indicate that glaucoma was present in 5.3 percent of all residents, a possible and potential glaucoma in 10.2 percent, and a normal tension in 84.5 percent. When considered by age groups as in the initial study in vision, remarkably little variation is seen in all the different decades. This observation is contained in Table 5.

These figures would seem to indicate a certain levelling of intraocular pressure in the older age groups. This is different from what one is led to expect from previous statistics. Duke-Elder[32] states that the onset of glaucoma increases with age from 50 to 70 years, but is less common after 70 years. In our studies the tendency to glaucoma remains fairly stationary at about five percent in all age groups over 65 years. There is a slight increase of about one to three percent in the possible and potential glaucoma group in the decades from 70 to 80 years and 80 to 90 years, but the number of eyes is too small to be statistically significant. This phase of the study is graphically represented in Chart 4.

If the entire series of eyes is divided into the two large groups below and above the age of 80 years, the figures for each classification remain essentially the same (table 6). If one examines the figures, the indications

TABLE 5

PERCENTAGE VARIATION IN INTRAOCULAR PRESSURE IN SUCCEEDING AGE GROUPS

	Age groups			
	60–69	70–79	80–89	90–over
(mm. Hg) Tension up to 25	85.4%	83.6%	85.4%	89.7%
Tension 26 to 30	8.7%	11.3%	9.6%	5.15%
Tension 31 and over	6.6%	5.1%	5.0%	5.15%
Number of eyes	242 eyes	956 eyes	658 eyes	39 eyes

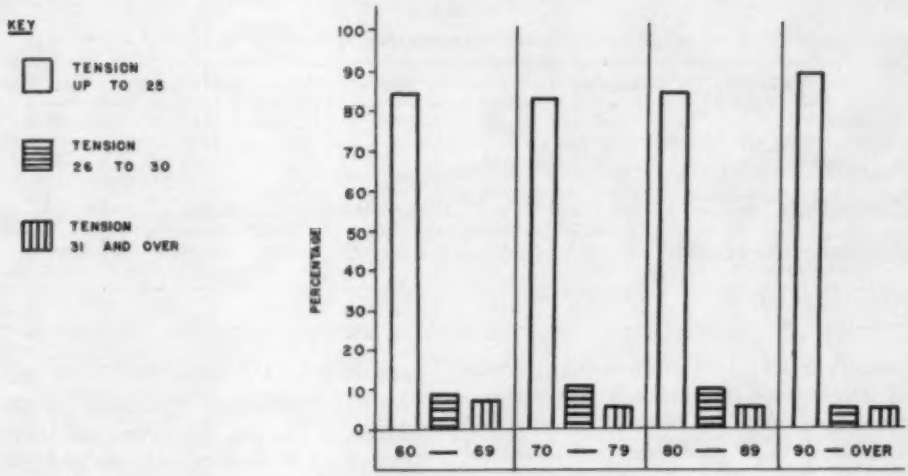

Chart 4 (Kornzweig, Feldstein, and Schneider). Percentage variation in intraocular pressure in succeeding age decades.

are that over the age of 80 years, there is slightly less tendency to glaucoma and preglaucoma, and more to normal tension than in the under 80 years group.

Scleral rigidity

In 1918 Bader[33] showed that the elasticity of the sclera as compared to the cornea decreases with age, especially after the age of 40 years. This increase in rigidity of the sclera is believed to be due to a loss of water and an increase in calcium in the tissue (Fischer[6]). In 1937 and again in 1949 and 1950, Friedenwald[34–36] reported on the use of this information in testing for glaucoma with the Schiøtz tonometer. Measurements were taken with two weights, a 5.5 gm. and 10.0 gm. weight, and the effects of the scleral rigidity on the ultimate reading estimated by reference to a normalizing chart.

TABLE 6

Percentage variation in intraocular pressure in under and over 80 age groups

	Under 80	Over 80
(mm. Hg.) Tensions up to 25	83.9%	85.6%
Tensions 26 to 30	10.8%	9.3%
Tensions 31 and over	5.3%	5.1%
Total eyes	1,200 eyes	697 eyes

An opportunity to study the effect of scleral rigidity on intraocular pressure was available in this survey. This portion of the report must be considered as a preliminary one, since it is necessary to repeat the test in doubtful cases at least four to six times. But some results which are interesting were obtained up to the time of the completion of this survey.

A total of 809 residents (1,618 eyes) were tested for scleral rigidity at least once. The measurements were taken with a 5.5 gm. weight and a 10.0 gm. weight with the Schiøtz tonometer. Of the total group, 564 eyes or 38.5 percent showed increased scleral rigidity and 89 eyes or 5.5 percent showed diminished scleral rigidity. The remainder of 653 eyes or 57 percent showed an insignificant variation of less than 3.0 mm. Hg between the two weights.

There were 58 eyes or 3.5 percent with definite glaucoma, that is, tension over 30 mm. Hg. In the possible or potential group—tension between 26 and 30 mm. Hg—there were 175 eyes. It is this group of

TABLE 7

MACULAR DISEASES

Type	Number	Male	Female	Under 80	Over 80	% of Total
Senile	247	95	152	127	120	78.6
Diabetic	35	15	20	19	16	11.1
Kuhnt-Junius disease	4	2	2	2	2	1.2
Myopic	9	5	4	5	4	2.86
Miscellaneous	19	7	12	12	7	6.0
Total	314	124	190	165	149	

patients on whom the diagnosis of glaucoma is only possible or potential that repeated tonometric tests are being done with two weights in order to determine the value of scleral rigidity tests for the diagnosis of glaucoma. The final report on scleral rigidity will be made when this phase of the work is completed.

MACULAR DISEASE

In studying macular disease, the question of classification is soon encountered. Not all authorities are agreed on how to classify all known abnormal states of the macula. But from the point of view of this statistical study, an exact and complete classification at this time is not essential. That will be considered in detail when a clinical and pathologic study of macular disease in the aged is presented. In Table 7, the number of patients with macular diseases in both eyes is shown, divided according to a broad classification and also according to sex and age group, either under or over 80 years. The percentage of macular disease in the entire group was 29.3 percent; in those under 80 years, 24.1 percent; in those over 80 years, 38.6 percent.

About 30 percent of the aged residents had disease of the macula in both eyes, which impaired vision to some extent. The expectancy for macular disease increases with the years as indicated by the greater percentage, 38.6 percent, of occurrence in the over 80 years group, as against 24.1 percent in the under 80 years group.

SUMMARY AND CONCLUSIONS

An ocular survey of 1,068 aged persons, residents of The Home for Aged and Infirm Hebrews of New York, was made. Visual acuity up to 15/70, considered good to adequate, was present in 86.1 percent and poor vision to no light perception was found in 13.9 percent. Good to adequate vision diminished about 10 percent in the age group over 80 years, while poor vision increased to a similar degree.

Cataract formation of all degrees was found in 61 percent of the entire group. Of the under 80 age group, 52 percent had some degree of cataract formation, but in the over 80 age group, this increased to 76 percent. Nevertheless, of the entire group, only 4.4 percent were actually operated upon for cataract.

Glaucoma was found in 5.3 percent of all residents. Intraocular pressure between 26 and 30 mm. Hg, possible or potential glaucoma, was present in 10.2 percent of all the persons studied. Normal tension was present in 84.5 percent. There does not appear to be any significant increase or decrease in glaucoma expectancy as the age of the individual increases above 70 years.

Disease of the macula is present in 29.3 percent of the residents studied in the survey. This percentage definitely increases with increasing age, being 24.1 percent under 80, and 38.6 percent over 80 years.

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A NEW PICTURE SERIES FOR PRESCHOOL VISION TESTING*

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Early vision testing has received increasing recognition[1] as the key to amblyopia prevention. Ophthalmologists have an educational responsibility to inform the general public in this regard.[2] Professional colleagues in general and pediatric practice must be indoctrinated and trained in the techniques of preschool vision testing. To provide this training, ophthalmologists must be familiar with the principles and the means of preschool vision testing.

The factors involved in visual acuity determination in children have been considered elsewhere.[3] Other things being equal, the success obtained in the use of any test will depend upon the examiner's understanding of the importance of the test and the factors involved in its administration. It appears that the illiterate E or the Sjøgren hand[4] offers the best method of testing children who can understand the idea of these tests. However, there are many children who cannot comprehend these tests but can be tested by the use of pictures. Gundersen[5] considers that most three-year-old children fall into the latter category.

The principal requirements for a preschool vision test are as follows:

1. The test must permit comparison of the child's two eyes with each other and with the vision of normal children in the same age group.

2. To be useful on a large scale, a vision test for young children must be capable of being administered and interpreted, not only by physicians, but also by lay persons such as technical assistants, preschool teachers, and volunteers.

These objectives can best be achieved through attention to the following considerations:

1. *Presentation of test characters individually.* Although the illiterate E is now commonly presented to children in isolated form, pictures have hitherto been offered only on graduated charts. Visual acuity involves utilization of the form sense, a sense imperfectly developed in young children. The use of charts is in conflict with the principle that the sense of form is most easily utilized when the test character is presented in an otherwise empty field.[6] Moreover, rapid memorization of shapes and locations of pictures on a chart may lead to falsely positive responses on testing the second eye.

2. *Use of pictures within the familiar experience of children.* Not only must the subject matter be familiar to the child but in so far as possible the pictures should awaken a pleasant emotional response in the child. Since children vary in their tastes, diversification of subject matter is also important.

3. *Variation of distance with age of child.* There can be little doubt that the visual functions are exercised at increasing distance with increasing maturity. A two-year-old child is seldom concerned with the recognition of detail across the street. Most three-year-old children will not take the trouble to decipher small characters at a distance of 20 feet. This is in accord with the fact that the visual acuity of three-year-old children is only partially developed. Experience indicates that 15 feet is a useful working distance for three-year-olds and that test objects of the 30-foot size are the smallest which can consistently be recognized by three-year-olds at 15 feet.

4. *Design of pictures for use at the test distance.* The intricacies of picture design for vision testing can only be appreciated by constructing several pictures of the same object and viewing these at the test distance. Not only outline, but the interior proportion of black to white is of the greatest impor-

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tance. Fine lines below the threshold angle disappear entirely. Thick lines appear as black blobs, especially at intersections. Repeated trial and error are necessary before a satisfactory picture can be produced.

5. *Correlation of picture recognition distances with known acuity levels.* The subjects having been chosen and the designs executed, maximum picture recognition distances must be correlated with know levels of visual acuity. Since the responses of individuals to these targets vary widely, only the maximum recognition distance for each picture can have validity. For a properly constructed series these maximum distances should be approximately uniform for each given level of acuity. This correlation must necessarily be carried out with older children or with adults.

6. *Control of illumination.* The factor of illumination, whose importance has been emphasized by Odland and Sloan,[6] is difficult to control in the case of a test intended for broad administration by nonprofessional personnel. For example, the services of teachers, volunteers, and the office assistants of pediatricians and general practitioners will be required if preschool vision testing is to proceed on a broad scale. It is therefore necessary to make the lighting arrangements as simple as possible and to leave estimation of visibility up to the subjective discrimination of the examiner. As a guide, however, it is suggested that the optimal requirement of 10 to 15 foot-lamberts will be met if the pictures are illuminated obliquely by a 75-watt bulb with metal reflector placed about five feet away from the pictures at an angle of about 45 degrees to the side and in front.

7. *Application of the test to preschool children under the conditions of use.* Finally it must be determined that children of the age group to be tested can recognize the pictures at the distance for which they are intended and that differences of acuity will be brought out by variations in the picture recognition distance.

A NEW TEST

Adherence to the above principles resulted in the development of a series of pictures designed to be incorporated, one to a side, as individual pages in a small ring binder.* The recognition facility of these pictures was made to correspond as closely as possible with that of the 30-foot E. Eight pictures (fig. 1) were selected from a much larger

* Manufactured by Ophthalmix, Inc., La Grange, Illinois.

TABLE 1

CORRELATION OF PICTURE RECOGNITION DISTANCES IN FEET WITH DIFFERENT ACUITY LEVELS (SNELLEN)

Patient	J. B.		L. J.		A. T.		G. G.		J. L.		P. C.	
Age	3½		4 10/12		7		38		28		30	
	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.
Snellen	—	—	—	—	20/20	20/30	20/15	20/30⁻	20/25⁺	20/70	20/15	20/100
Cake	20	20	20⁺	16	20⁺	15	30	14	20	6	30	7
Tulip	20	20	16	9	20⁺	11	30	8	23⁺	7	30	6
Panda	20	20	6	—	20⁺	15	30	18	23⁺	5	30	5
Jeep	20	20	20⁺	16	20⁺	17	30	18	23⁺	9	30	4
Horse	20	20	20⁺	10	20⁺	14	30	10	20	10	30	7
Tree	20	20	20⁺	15	20⁺	15	30	18	23⁺	8	30	6
Phone	20	20	20⁺	16	20⁺	14	30	20	21	7	30	5
House	20	20	18	13	20⁺	15	30	15	21	4	30	7
30' E	15	15	20⁺	16	—	—	30	18	23⁺	12	30	6
	Normal	Normal	Normal	Amblyopic	Normal	Amblyopic	Normal	Amblyopic	Old retinitis	Organic retinal disease	Normal	Amblyopic

Fig. 1 (Allen). Preschool vision test characters. Actual size with 30-foot E.

series as a result of their interest value for preschool children and the consistency of their recognition distances. Extensive trials have shown that these pictures can be recognized at 15 feet by normal three-year-olds and at distances up to 20 feet by four-year-old children. Differences of even one line in Snellen acuity are reflected in corresponding shortening of recognition distances (table 1). The subject matter, the construction of the drawings, their presentation individually, and their correlation with known acuity levels are considered to represent improvements over picture charts in current use. Instructions for administration are included with the test.

Comment

The test is not intended to replace but to complement existing tests like the illiterate E and the Sjøgren hand. It is recognized that the latter tests are undoubtedly superior and better standardized for children who can use them.

Every ophthalmologist has encountered children up to five years old who seem unable to understand the idea of designating the four positions of the illiterate E. Moreover, pediatricians and general practitioners do not always have time to drill children in the technique of this test. For these children and practitioners it is hoped that a picture test based on rational principles and tested in practice will find at least a limited range of usefulness.

Summary and Conclusions

1. The high incidence of amblyopia indicates the need for vision testing in preschool children three years old and older.

2. Ophthalmologists have the responsi-

bility for educating the public and the medical profession in amblyopia prevention.

3. Because of extraocular influences, results of acuity testing in young children must be regarded merely as minimum values.

4. Unsatisfactory tests should be repeated at monthly intervals, until definite results are obtained.

5. The illiterate E is recommended as the most useful test for children who can comprehend it.

6. A new picture test, for children who cannot master the illiterate E, is described and correlated with a 30-foot denominator.

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OCULAR TOXOPLASMOSIS

Report of cases

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Toxoplasma gondii, the causative agent in toxoplasmosis, first was reported as a new protozoon species in 1909,[1] and the early literature on toxoplasmosis has been well reviewed.[2] Three decades passed, however, before human toxoplasmic infection of the choroid and retina came to be recognized. Thereafter, the interest of ophthalmologists in toxoplasmosis as a cause of chorioretinitis waxed and waned until 1952 when the reports of Wilder[3,4] highlighted its significant etiologic role.

In April of that year she reported 41 cases of chorioretinitis in which Toxoplasmalike organisms were found microscopically at the Registry of Ophthalmic Pathology in Washington. Four months later she reported finding additional cases in which these organisms were present in lesions of retinochoroiditis in patients ranging in age from 14 to 83 years at the time of enucleation of the eye. The histologic diagnosis of toxoplasmic retinochoroiditis was confirmed in many of these patients by serologic tests for toxoplasmosis, performed by Woods, Jacobs, Wood, and Cook.[5] The resulting renewed interest reflected in recent literature, and particularly the stimulating editorial by Cassady[6] in a recent issue of the American Journal of Ophthalmology, prompted the reporting here of a small series of cases believed to be of toxoplasmic origin.

Probable sources of infection

In reviewing 113 cases of toxoplasmosis reported in the literature, Barnett, Lebhar, and Longworth[7] noted that animal contacts were mentioned in 36. In their case of congenital toxoplasmosis the mother during her pregnancy had been in contact with a sick cat. When toxoplasmic infection was discovered in the child soon after birth, the cat was killed and at autopsy small granulomas were found in the heart and brain.

Cole, Prior, Docton, Chamberlain, and Saslaw[8] studied families exposed to their Toxoplasma-infected pet dogs and established an association between Toxoplasma-shedding chronically infected dogs and the occurrence of proved human infection. Their

observations of concurrent human and animal toxoplasmosis tend to strengthen the contention of numerous investigators that animals are a probable source of toxoplasmosis in man.

In a study in England, Beverley, Beattie, and Roseman[9] found by the dye test that Toxoplasma antibodies in titers of 1:4 or more were present in the sera of 24 percent of a sample of adult population of Sheffield. Significantly higher, with regard to strength as well as number, were the reactions of the sera of veterinary surgeons and abattoir workers, and even higher were the reactions of the sera of those who handled rabbits. Those of rabbit trappers were highest of all.

Toxoplasma antibodies active to a titer of 1:40 in the dye test were found in 34 percent of wild rabbits and to a titer of 1:160 in five percent. Sabin[10] named dogs, cats, wild rats, pigs, sheep, goats, cattle, rabbits, guinea pigs, pigeons, and chickens as proved carriers. He concluded that Toxoplasma gondii, the protozoon parasite originally recovered from the North African rodent, the gondii, is present in most parts of the world, and by a variety of means is naturally transmitted among many animals and certain birds, and seemingly also to hundreds of millions of human beings.

Pathologic process

Retinochoroiditis or granulomatous uveitis follows the release of encysted Toxoplasma organisms in the retina.[2] These organisms incite an endophthalmitis either adjacent to old healed lesions or as a new manifestation of retinitis. Their dormant state explains long periods of inactive retinochoroiditis, which flares up sometimes years after the initial infection and at a time when the antibody titer is low. Although this process can be a residuum of congenital toxoplasmosis and the organism may remain encysted for years, its mode of transmission remains unknown.[6,11] Sabin[10] recently reviewed observations of various authors which, taken together, provide strong support for Frenkel's hypothesis that adult ocular toxoplasmosis may represent an allergic inflammatory response to ruptured pseudocysts.

Diagnosis

The cytoplasm-modifying antibody test, using methylene blue dye, described by Sabin and Feldman[12] in 1948, proved to be a noteworthy contribution in diagnosing and following the results of therapy in the infection caused by this human pathogen, which may be lethal for both infants and adults.

Cassady[6] observed that on the basis of his experience with the dye test and that of other recent authors cited by him, 25 percent to 40 percent of retinochoroiditis in adults is probably due to infection with Toxoplasma. He advised re-evaluation of this diagnostic aid, entered a plea for its increased availability, and urged that it be employed in determining the etiology of granulomatous uveitis or retinochoroiditis. To complete the clinical survey after other causes of uveitis have been ruled out, he advocated utilization of both the intracutaneous toxoplasmin test and the Sabin-Feldman dye test.

In 1952, Weinman[13] concluded that "the relation of positive skin and low titer serologic tests to Toxoplasma infection is conjectural. If these are taken at their face value to signify infection, then toxoplasmosis is one of the commonest infections of man—a conclusion which cannot justifiably be drawn on present evidence."

That same year, Humphries and Grulee[14] reported a study in which 102 infants and children were examined for the Toxoplasma antibody, the dye test being used. Also, 41 patients had skin tests with an antigen made from mouse peritoneal exudate. In five patients the reaction to the dye test was negative, but positive to the skin test. Attempted correlation of the disease which brought the patient to medical attention and laboratory evidence of toxoplasmosis led to a presumptive relation being suspected in a few instances.

The majority of the children, however,

with either significantly high titers or positive reaction to skin tests exhibited no recognizable clinical manifestations of toxoplasmosis. The authors concluded that the demonstration of the Toxoplasma antibody and/or a positive reaction to tests for dermal sensitivity to mouse antigen in children suspected of having the disease should be considered of limited diagnostic value. They did so because 25 percent of subjects chosen at random show positive reactions to dye tests and because a disturbing lack of correlation between the two tests exists.

Frenkel and Friedlander[3] noted that in the majority of their cases in which chorioretinitis was active and the reaction to the skin test was positive, the dye test titers were only moderately high, the median titer being 1:32. In their report of a series of 409 cases in which the dye test was performed, Woods, Jacobs, Wood, and Cook[5] observed that in old quiescent cases of probable ocular toxoplasmosis, the dye test was usually of moderate titer (1:64 to 1:256).

Results of this test in 58 of 201 cases of granulomatous uveitis were sufficiently positive to indicate a toxoplasmic etiology. In one group in which a previous medical survey had given no indication of a causative factor, the dye test gave positive results in 56 percent. These authors concluded that, subject to the fallacies of the dye test, adult ocular toxoplasmosis is an actual clinical entity, that if is the probable cause of adult granulomatous uveal disease in 25 percent of cases, and that a diagnosis of toxoplasmic chorioretinitis can be made only by correlation of the ocular picture, the results of a careful medical survey to exclude other possible causes, and the results of serologic tests for toxoplasmosis. In view of their estimate of incidence, it would appear, as Cassady, Culbertson, and Bahler[11] observed, that toxoplasmosis in the adult is a widespread and common infection, although rarely manifested systemically, and that the parasite has an affinity for ocular tissue.

A noteworthy evaluation of the intracutaneous toxoplasmin test, the dye test, and the complement fixation reaction for toxoplasmosis in the diagnosis of various forms of uveitis was presented by Jacobs, Naquin, Hoover, and Woods[15] at the April, 1956, Clinical Meeting of the Wilmer Residents Association of the Wilmer Ophthalmological Institute. These authors, after reviewing the results of the earlier study by Woods and his associates,[5] observed:

"It is now generally conceded that acquired toxoplasmosis is an important cause of adult granulomatous uveal disease, and that the skin and dye tests are usually positive in these patients. However, while the evidence for these generalities is conclusive, nevertheless, in the individual clinical case, it is extremely difficult to evaluate the significance of the positive cutaneous and serologic tests, and there is no generally accepted criterion for a firm clinical diagnosis of acquired adult ocular toxoplasmosis.

"The difficulties arise from the relatively high incidence of positive results in apparently normal healthy individuals, the possible non-specificity of the dye test, the improbability of isolating the parasite from the blood or extraocular tissues, and the absence of any associated systemic symptoms of infection with the parasite."

The diagnostic criteria employed by these authors for the diagnosis of ocular toxoplasmosis in their series of 193 adults, of whom 86 had the nongranulomatous and 107 had the granulomatous form of uveitis, were:

1. An ocular picture believed to be compatible with ocular toxoplasmosis, that is, a focal chorioretinitis, old glial scars with a superimposed acute allergic reaction, a generalized uveitis, or a retinal periphlebitis.

2. The exclusion of other systemic granulomatous infections to which the uveitis logically could be attributed.

3. The presence of a positive reaction to the intracutaneous toxoplasmin test and also to the dye test in a minimum titer of 1:64.

Details of the extensive medical survey

carried out in each instance to determine, if possible, the specific cause of the ocular disease were described by Woods.[16] Jacobs and his associates[15] were of the opinion that it would be unwise to reduce below 1:64, or at least no lower than 1:32, the required titer for a significant dye test until the situation is clarified, if a diagnosis of adult ocular toxoplasmosis is to be made in any given case of active ocular disease.

The incidence of positive results in skin testing and dye tests in the group with granulomatous uveitis in this series was strikingly higher than in the group with the nongranulomatous form of the disease. Apparently the complement fixation test is too insensitive to be of diagnostic aid, for this study showed it to be of little or no value unless a positive reaction developed during the course of an acute infection.

In evaluating the significance of one test giving positive results and the other negative results, these investigators observed that since it is known that skin sensitivity develops later than serum antibodies, this explanation might account for some of the discrepant results in individual patients if there were some evidence of recently acquired infection.

They were of the opinion, however, that more investigation is needed before general statements are warranted concerning the relative persistence of serum antibodies and skin reactivity. Their figures indicated that the intracutaneous toxoplasmin test is an excellent screening test, and they estimated that in granulomatous uveitis the margin of error varies from five to 15 percent according to the standard used for a positive result in the dye test.

They noted "an apparent higher incidence of strong skin tests and high titer dye tests in the group supposed to have acute ocular toxoplasmosis." These observations were "in line with Frenkel's contention that there are two general patterns of ocular toxoplasmosis, each with a somewhat different type of immune response."

They reported that these are:

"A. Acute infections, when the skin test may at first be low, but soon becomes strongly positive. The dye test is usually positive in high titers; the complement fixation test is variable, but it may become positive and reach high titers.

"B. Chronic infections, when the toxoplasmin test is positive, but only of moderate intensity. The dye test is positive, often in low titers, and the complement fixation test is usually negative."

Recently, Hogan[17] in his review of a conference at the National Institutes of Health relating to the diagnosis of ocular toxoplasmosis, cited Frenkel as stating that he would be willing to accept an induration of 5.0 to 6.0 mm. with erythema of 10 to 20 mm. as a positive skin test in the absence of reaction at the control site. He added that Frenkel "presented evidence that skin testing causes a significant anamnestic rise in the dye test titer of many persons. Jacobs and Feldman had not observed such changes, using different antigens and/or time intervals."

In reply to an inquiry by Dr. James N. Patterson, a local pathologist, at my request, Feldman[18] wrote:

"We have never been able to demonstrate that a Toxoplasma skin test performed with antigen produced from infected chick embryos has any effect on the dye test titer. This has also been true of most experience with mouse antigen, although there is one investigator who claims that the latter material will produce a rise in dye test antibodies."

Goldman,[19] reporting recently from the Toxoplasma Diagnostic Laboratory of the Communicable Disease Center of the U. S. Public Health Service at Chamblee, Georgia, stated that in trying to set up a routine for running the dye test for toxoplasmosis, it had been his experience and also the experience of other authors in widely different areas that results were often erratic and unpredictable.

He attributed the major variations in dye test results in his laboratory to inherent variability of the peritoneal exudate, which is obtained from infected mice, rather than to technical error. Also, he suggested ways by which the dye test might be better standardized for routine use in diagnostic laboratories.

Since the dye test still remains to a considerable extent a research laboratory procedure, skin tests are not fully standardized, and sufficient information is not available on correlation of dye and skin tests, the diagnosis of toxoplasmosis at present rests on a combination of factors and often must remain presumptive. A dye test giving a positive result in a low titer is no more diagnostic of toxoplasmosis than is a positive reaction to an intracutaneous toxoplasmin test.

The characteristic ocular picture, history, clinical examination, intracutaneous toxoplasmin test, dye test, and even a therapeutic test are all important diagnostic criteria. A trial of accepted therapy without improvement of the condition might have more diagnostic value than one with improvement since it would indicate that toxoplasmosis probably was not present. If improvement did occur, however, one might argue that a causative agent other than T. gondii may have responded to this type of therapy.

Report of cases

Case 1

R. E., a white woman, aged 18 years, complained in September, 1949, of poor vision in the left eye for 10 years, which had deteriorated greatly within recent weeks. Her father had lost the sight of the left eye from unknown cause prior to his death at the age of 35 years.

On funduscopic examination, a quiescent lesion of chorioretinitis about four disc diameters in size with large pigmented borders was observed in the right eye above the disc. In the left eye, multiple large areas of chorioretinitic scars with much pigment deposition in the macula and surrounding area were observed. In one lesion activity was manifested by marginal edema, slight elevation, and an exudative vitreous haze in the area. The vitreous in this eye exhibited haze of considerable degree with many granulations and thinning of structure.

The vision in the right eye was 20/30, unimproved with corrective lens, and the accommodative effort was normal. In the left eye it was 8/200, unimproved, and a J20 was not obtained at near. The visual field was fairly normal for form and color, with a defect below in the right eye, while in the left eye there was a concentric contraction for form and color with a large central scotoma. The intraocular pressure in both eyes was 16 mm. Hg (Schiøtz).

General physical examination, roentgen studies of the chest and skull, complete blood and spinal fluid examinations, the Kahn and Mazzini tests, and the intracutaneous and serologic agglutination tests for brucellosis gave negative results. Reaction to the intracutaneous tuberculin test was positive locally. The Sabin-Feldman dye test for toxoplasmosis, performed at the laboratory of Dr. Harry A. Feldman in Syracuse, New York, on a specimen forwarded by Dr. Patterson, was reported by Dr. Feldman as giving negative results.

The patient went to college shortly after I saw her, and at my suggestion received there an adequate course of dihydrostreptomycin and Promizole by mouth, followed by injections of old tuberculin. At appropriate intervals she continued to consult me. By late December, 1950, the posterior lesion in the left eye had become completely inactive and at that time the intracutaneous tuberculin and brucellergen tests gave negative results.

Free of ocular complaints and in good health for more than four years, she did not return again until January, 1955, complaining of sudden clouding of vision in the right eye two weeks previously concurrently with the onset of a sore throat. In the right eye activity of considerable degree was present posteriorly in the paramacular region below with edema, slight bleeding, and corresponding vitreous haze; the vitreous showed many fine opacities.

Anteriorly, a few fine keratic precipitates below were observed. The vision in this eye was 20/50, unimproved. The lesions in the left eye were quiescent, and the vitreous pattern was fairly normal.

The intracutaneous tuberculin and brucellergen tests gave negative results at this time. The intracutaneous toxoplasmin test, however, was strongly positive for Toxoplasma. Slight elevation of temperature and malaise also indicated a questionable general reaction and increased vitreous haze in the right eye suggested some focal reaction. A complete physical examination, again including roentgenograms of the skull and chest, gave negative results.

Treatment consisted of pyrimethamine (Daraprim), 25 mg. three times a day; Combisul-TD, one gm. three times a day; sodium Sulamyd solution (30 percent) administered locally every two hours in the eye manifesting active disease, and sulfathiazole ointment in this eye twice daily with a cycloplegic in the eye on each office visit. Results were so spectacular that within four weeks the vision again was 20/30 in the right eye. A small healed lesion was below the macula in this eye with a single pigmented area in the center of the scar. Otherwise the funduscopic picture in the

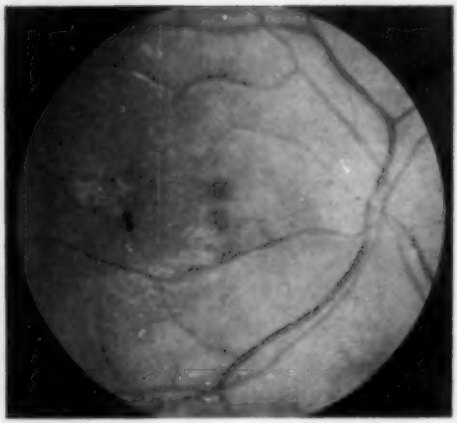

Fig. 1 (Forbes). *Case 1.* Fundus of the right eye after an acute attack of uveitis in 1955, showing paramacular scarring and pigment deposition.

two eyes was not altered (figs. 1 and 2).

Oral therapy was continued for six weeks. In the 18 months that have elapsed since that time there has been no change in the funduscopic pattern except for somewhat heavier deposition of pigment in the paramacular region. The Haidinger brush test on the right eye continued until recently to result in no recognition of the target.

Latest studies of the central fields indicated an absolute paracentral scotoma above fixation with a one-mm. target. Reaction to intracutaneous toxoplasmin tests in July and August was weakly positive. The Sabin-Feldman dye test, performed at the South Bend Medical Foundation in South Bend, Indiana, in November, was reported to Dr. Patterson by Dr. Carl S. Culbertson as giving a positive result in a dilution of 1:64.

In January, 1956, the reaction to the intracutaneous toxoplasmin test was weakly positive. Six months later, the vision in the right eye was 20/30, and the Haidinger brush test elicited a normal response in the right eye. In August, the response to the intracutaneous toxoplasmin test again was weakly positive.

Comment

In this case of long-standing recurrent posterior uveitis, there was binocular evidence of posterior fundal lesions typical of toxoplasmosis in 1949 at the time of an acute uveitis in the more involved left eye, although the Sabin-Feldman dye test gave negative results. At that time the reaction to the intracutaneous tuberculin test was positive.

Five and a half years later, at the time of an acute flare-up of a dangerously located active lesion in the one functioning right eye, reaction to the intracutaneous toxoplasmin test gave positive results locally, and possibly focally and generally. The intracutaneous tuberculin test now gave negative results. The reaction to the dye test, originally negative, was positive following the flare-up of the ocular disease.

The response to the accepted therapy for uveitis caused by Toxoplasma was dramatic, and useful central vision in the one functioning eye probably was salvaged. This result would seem to warrant the institution of this type of treatment of posterior uveitis when toxoplasmosis is strongly suspected in the absence of a positive reaction to the dye test. The treatment also is indicated when many factors suggestive of this disease, such as roentgen evidence of pulmonary or intracranial changes, are absent, but the reaction to the intracutaneous toxoplasmin test is positive.

Case 2

T. M., a white boy, aged 15 years, complained in March, 1955, of headaches associated with nausea, occurring periodically with no fixed time of onset. On previous ocular examination elsewhere, he had been told he had scars in the back of his eyes.

Significant findings observed were heavily pigmented quiescent lesions of chorioretinitis in both eyes, distributed particularly in the lower halves of the fundi, and in the right eye evidence of a residual Cloquet's canal. Vision was 20/20 in each eye with little refractive error.

General physical examination, including roentgenograms of the skull and chest, gave negative results. Reaction to the intracutaneous tuberculin and toxoplasmin tests was negative. The intracutaneous brucellergen test gave moderately positive results locally. Reaction to the agglutination test for brucellosis was negative. The parenteral histamine test gave positive results.

Treatment consisted of Distrycin parenterally, tetracycline and nicotinic acid orally, and histamine at first sublingually and later parenterally, with complete relief of the headaches. In June,

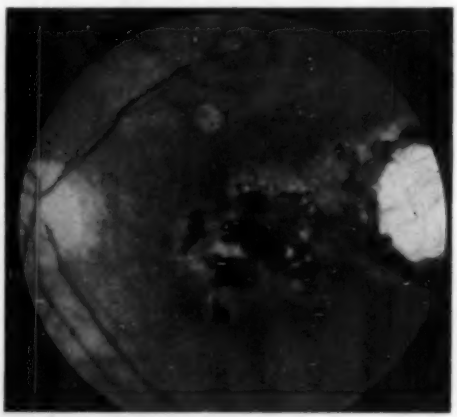

Fig. 2 (Forbes). *Case 1.* Fundus of the left eye in 1955, showing multiple large lesions of long duration.

there was a negative reaction to both the intracutaneous tuberculin and brucellergen tests.

In March, 1956, in addition to a positive reaction to the intracutaneous test for brucellosis, there was a positive reaction locally to the intracutaneous toxoplasmin test. Response to the intracutaneous tuberculin test remained negative. The result of the dye test was reported positive in a dilution of 1:32 by the South Bend Medical Foundation.

A course of Daraprim and Combisul (3) was prescribed, combined with Distrycin parenterally, streptomycin drops locally and a sulfonamide ointment in both eyes on retiring. The patient did not tolerate the medicine well, and it was decided to postpone treatment until summer vacation.

One month later, however, he complained of blurred vision in the left eye. Vision in this eye was 20/40. There was activation of one large chorioretinal lesion to the nasal side of the disc below with many vitreous opacities and a few keratic precipitates on the lower portion of the cornea. Intracutaneous tests for tuberculosis, brucellosis, and toxoplasmosis all gave positive results, the last showing greatest reaction.

Daraprim and Combisul (3) orally, iontophoresis with sodium Sulamyd solution 30 percent, and streptomycin in the left eye, and also Cortrophin-Zinc, one cc. every third day, sodium Sulamyd eyedrops, and a sulfathiazole ointment were the therapeutic measures employed. Within two weeks the eye was clear and has remained so, and the vision now is 20/20 in this eye. In July the reaction to the intracutaneous toxoplasmin test was positive; to the dye test, positive in a dilution of 1:256; and to the intracutaneous tuberculin and brucellergen tests, negative.

Comment

In this case it is noteworthy that in March, 1955, reaction to the intracutaneous tuberculin and toxoplasmin tests was negative, but positive to the intracutaneous test for brucellosis. In April, 1956, however, it was positive in all three tests at the time of an active flare-up of the chorioretinitis in the left eye, and the result of the dye test was positive in a dilution of 1:32. The prompt response to therapy directed at infection with Toxoplasma suggests toxoplasmosis as the causative factor.

Case 3

L. P., a white woman, aged 22 years, complained in March, 1951, of blurred vision for three months in the left eye. There was a personal and family history of migraine. In the upper nasal side of the right eye a fundal lesion of old chorioretinitis with much marginal pigment, four or five times the disc diameter in size, was present.

A lesion similar in size and appearance was located temporally above in the left eye. Activity was present in this lesion with blurring, elevation, some bleeding of one margin, many vitreous opacities, and some keratic precipitates below. There was a high refractive error in both eyes with a corrected vision of 20/20 in the right eye and 20/50 in the left.

General physical examination, including roentgenograms of the skull and chest, gave negative results. The intracutaneous tuberculin test gave moderately positive results locally with little general and no focal reaction. The intracutaneous brucellergen test gave negative results. Home therapy prescribed consisted of atropine, penicillin, and streptomycin eye baths and a Cortone ointment. Office treatment included penicillin and streptomycin iontophoresis and Cortone administered subconjunctivally.

During the next four years three episodes of posterior activity occurred in the left eye, with old tuberculin injections used at one time, staphylococcus toxoid at another, and staphylococcus-streptococcus vaccine the third time. By March, 1956, the reaction to the intracutaneous tuberculin test had been positive twice and negative seven times; to the brucellergen test negative five times.

The intracutaneous toxoplasmin test, however, gave a moderately positive result locally although the reaction to this test had been negative three times previously and a course of Daraprim and Combisul (3) had been given late in 1955 when there was some activity in the left eye. The dye test in March, 1956, gave a positive result in a dilution of 1:64.

The present ocular condition is satisfactory with corrected vision of 20/20 in both eyes. The eyes are quiescent posteriorly, and few vitreous opacities are present. The left eye seemed to show its greatest improvement after the treatment for toxoplasmosis.

Case 4

H. R., a white woman, aged 28 years, was first seen in March, 1956, complaining of blurred vision in the right eye since 1951, with an increase in blurring for one week prior to consulting me. She had been treated by other ophthalmologists during this four-year interval without apparent improvement.

A large chorioretinal scar in the right eye somewhat paracentrally placed and to the temporal side, showing marginal pigment and some activity above, was approximately 2.5 disc diameters in size. There also was a massive vitreous haze. Vision was 6/200 in this eye and 20/20 plus in the left eye. A questionable central scotoma was elicited in the right eye. The intraocular pressure was 16.9 mm. Hg (Schiøtz) in both eyes.

General physical examination and roentgenograms of the chest and skull gave negative results. Reaction to intracutaneous tests was moderately positive locally to old tuberculin and to brucellergen, but much more so to toxoplasmin. The result of the dye test was positive in a dilution of 1:128.

Daraprim and Combisul (3) orally and Distrycin parenterally were prescribed, along with streptomycin eyedrops and a sulfathiazole ointment for the right eye. Office treatment consisted

of iontophoresis with streptomycin and sodium Sulamyd solution 30 percent. Within one month the vision in the right eye had increased to 20/100— with slightly eccentric fixation. The central scotoma had decreased in size.

By late August, the eye had quieted down completely, and the corrected vision at that time was 20/30—1. Reaction to the dye test was now positive in a dilution of 1:256. The inflammatory process doubtless had been active in this eye since 1951.

CASE 5

J. C., a white boy, aged 15 years, consulted me in February, 1956, complaining of blurred vision in the left eye of at least five months' duration. The amblyopia had been discovered by accident in September, 1955, in the course of a routine ocular examination elsewhere.

In the right eye there was a large chorioretinitic scar above to the nasal side with much marginal pigment. The lesion was quiescent, and some vitreous thinning and granulations were present. Vision in this eye was 20/20. A large central and paracentral lesion with heavily pigmented margins to the lower temporal side of the left eye showed some activity, and there undoubtedly was a retinitic optic atrophy. Vision was 2/200 in this eye.

The intracutaneous tuberculin and brucellergen tests gave negative results, but the reaction to the intracutaneous toxoplasmin test was positive with some vesiculations and some focal and general reaction. The dye test gave a positive result in a dilution of 1:64. The general physical examination, including roentgenograms of the chest and skull, gave negative results.

Daraprim and Combisul (3) orally were prescribed, also sulfathiazole drops and ointment in the affected eye and atropine. Within three months the left eye was quiescent, and there were few vitreous floaters. A mild folic acid deficiency associated with the therapy was determined on routine blood examination, and folic acid orally was prescribed with satisfactory response.

Uninterrupted progress continued in this left eye, and in July, 1956, it was perfectly quiescent, with the vision improved to 20/200. At that time the intracutaneous toxoplasmin test gave a positive result; one month earlier the response had been negative, but to the dye test was positive in a dilution of 1:256. The intracutaneous tuberculin and brucellergen tests gave negative results.

CASE 6

H. F., a white woman, aged 45 years, had noticed blurring of vision in the right eye for four months when she consulted me in October, 1950. She complained of seeing through a cloud, which obscured vision in varying degree, and of seeing black spots in front of the left eye.

An extensive old area of chorioretinitis, somewhat active, was present to the temporal side and above in the right eye, and there were many fine vitreous opacities. In the left eye some vitreous thinning and granulations were observed. Vision in the right eye was 20/60, and in the left eye 20/20. The reaction to the intracutaneous tuberculin test was moderately positive locally. The intracutaneous brucellergen test and the Kahn test gave negative results.

Excellent recovery followed steroid therapy, iontophoresis with penicillin and streptomycin, and atropine locally. In March, 1952, the corrected vision in the right eye was 20/20, the fundus was quiescent, and the vitreous opacities were moderate in number.

When the patient returned in September, 1955, large flat keratic deposits were present in the right eye, and massive vitreous opacities made the viewing of the fundus almost impossible. The Hruby lens showed many thickened vitreous strands. The intraocular pressure in this eye was 14.2 mm. Hg and in the left eye 20 mm. Hg (Schiøtz).

The general physical examination, which included roentgenograms of the chest and skull, gave negative evidence. Intracutaneous tuberculin and brucellergen tests gave negative results. The reaction to the intracutaneous toxoplasmin test was moderately positive locally, and the dye test gave a positive result in a dilution of 1:126.

Treatment consisted of Daraprim and sulfadiazine orally, drops of atropine and sodium Sulamyd solution 30 percent, sulfathiazole ointment, and iontophoresis with sodium Sulamyd and streptomycin. In November, there was a positive reaction to the intracutaneous toxoplasmin test. The eye improved until January, 1956, when the lens became very intumescent and opaque, and an acute attack of secondary glaucoma occurred. The glaucoma was controlled by placing Mecholyl crystals in the lower fornix on two occasions and the administration of Diamox parenterally.

An iridectomy was planned, but as the intraocular pressure had decreased to 20 mm. Hg (Schiøtz), a combined intracapsular extraction was performed, with the eye reacting well. Treatment with Daraprim, sulfadiazine, and Diamox was continued. At that time the intracutaneous tuberculin and brucellergen tests gave negative results, and the response to the toxoplasmin test was positive.

One month later, the dye test gave a positive result in a dilution of 1:512. In April, on funduscopic examination, the scar of the inflammatory lesion was much larger than in 1951, the pathologic change in the vitreous was not excessive, the keratic deposits had practically disappeared, and the visual fields showed a considerable degree of constriction. The vision corrected to 20/100. In August, with an aphakic lens, the vision corrected to 20/40— in this eye. At near, a J5 was obtained with the presbyopic addition. Fortunately, the chorioretinitic lesion was far out to the temporal side of the macula.

CASE 7

E. R., a white man, aged 24 years, complained in 1941 of blurred vision in the right eye and the seeing of spots in both eyes. There was a high

refractive error, particularly in the right eye. Vitreous opacities were present in both eyes, especially in the right eye, and also multiple scars of chorioretinitis, below in the right eye and above in the left eye.

The vision was corrected to 20/50 in the right eye and 20/30 in the left eye. The reaction to the intracutaneous tuberculin test was positive with some vesiculation. The intracutaneous test for brucellosis gave negative results.

The patient was seen with some regularity until 1955, and during that period had received rather complete desensitization with old tuberculin injections and a course of dihydrostreptomycin parenterally. In March, 1955, mild chorioretinitic activity in the right eye quieted down rapidly under treatment with Daraprim and Combisul (3) orally, and a sulfathiazole ointment twice daily in the affected eye. At that time the reaction to the intracutaneous tuberculin and brucellergen tests was negative, but positive locally to the intracutaneous toxoplasmin test. The result of the dye test was positive in a dilution of 1:64.

In April, 1956, the corrected vision was 20/30 in each eye. There were multiple chorioretinitic scars and long stringy vitreous floaters in the right eye. In the left eye an epipapillary area of slight proliferation and fine vitreous floaters was present in addition to many scars of choroiditis, some heavily pigmented. The intracutaneous tuberculin and brucellergen tests gave positive results. The reaction to the intracutaneous toxoplasmin test was positive, and the response to the dye test was positive in a dilution of 1:32.

Comment

The question arising in this case is whether the ocular pathologic changes were of tuberculous or toxoplasmic origin or whether they were caused by a combination of tuberculosis and toxoplasmosis.

Case 8

O. E., a white infant, aged four months, was examined in October, 1953. The complaint was dancing of the eyes and apparent difficulty in seeing. The child had been ill at the age of two months with a temperature of 103°F. The mother, a twin, had experienced no illness during pregnancy. She had been advised that the infant's trouble was due to prenatal infection.

Ocular examination showed a coarse focusing nystagmus, corneal measurements of 10.75 mm. in each eye, an alternating esotropia of considerable degree, and sluggish pupillary reactions. Extensive fundal lesions to the temporal side of the macula and below were four to five disc diameters in size and had a considerable amount of pigment in the margins.

The definite symmetry of the lesions in the paramacular region and extending into the temporal periphery suggested a coloboma or other congenital developmental defect as well as toxoplasmosis. There was some pallor of both discs, but the vitreous appeared normal. The refractive error was one of high myopia. The intraocular pressure was 29.2 mm. Hg (Schiøtz) in both eyes under deep inhalation anesthesia. Through Dr. Michael Hogan of San Francisco the toxoplasmin for skin testing used in suspected cases of congenital toxoplasmosis was obtained from the Toxoplasma Laboratory of the Communicable Disease Center of the U. S. Public Health Service at Chamblee, Georgia.

Reaction to the intracutaneous toxoplasmin test was positive locally, and the dye test gave a positive result in a dilution of 1:512. Roentgen studies of the chest and skull gave negative evidence. No treatment was prescribed as the child was under the care of a competent pediatrician.

A four-mm. recession of the internal rectus of the left eye was performed in December, 1953, and in the right eye in May, 1954. In November refraction was done and a glass prescription given, also again in June, 1955. At that time the prescription was: O.D., —3.0D. sph. ⊃ —4.0D. cyl. ax. 180°; O.S., —9.0D. sph. ⊃ —3.0D. cyl. ax. 180°.

The intracutaneous reaction to old tuberculin and to toxoplasmin was positive, but negative to brucellergen. In March, 1956, the child was taken to the Ocular Research Unit, Walter Reed Army Hospital, Walter Reed Army Medical Center. A portion of the report, made by Lieut. Col. Jack W. Passmore (MC), U. S. Army, follows:

"This letter is to notify you of the outcome of the Sabin-Feldman dye test for toxoplasmosis performed on your daughter and on your wife March 6th of this year. If you remember, my diagnoses of your daughter's condition were (1) compound myopic astigmatism, bilateral, with anisometropia, (2) esotropia, and (3) bilateral paramacular lesions with no activity, etiology either congenital toxoplasmosis or macular coloboma.

"The dye tests were positive in both your daughter and in your wife. In your daughter, it was positive in a titer of 1:65,536; while in your wife, it was positive at a dilution of 1:4,096. These are unusually high. In fact, I have never seen one higher than that found in your daughter. Although this cannot be considered proof-positive, I do not think there is much doubt but that what your daughter's condition represents is one of congenital toxoplasmosis."

In spite of the positive findings, in the absence of activity of the lesions no specific therapy was advised.

Comment

In this case, in which a diagnosis of congenital toxoplasmosis is believed to be warranted, the exceedingly high titer of 1:65,536 in the dye test is noteworthy. It is also of interest that the maternal uncle of this child, a twin to the mother, has been under my care for an active discrete macular lesion in one eye. The dye test gave negative results in this case on three occasions as did the intracutaneous toxoplasmin test.

CASE 9

W. D., a white girl, aged 17 years, complained in April, 1956, of a film over the left eye for several days. There was a history of the mother having been fed largely intravenously during pregnancy.

In the right eye there were multiple scars of choroiditis with much marginal pigment. The lesions were inactive, and the vitreous was normal. Much exudate in the vitreous and many fundal scars with heavy marginal pigment were present in the left eye. Two of the lesions to the temporal side of the macula and below were active. Vision was 20/20+ in the right eye and 20/50 in the left eye.

The general physical examination and roentgenograms of the chest and skull gave negative evidence. The reaction to the intracutaneous tuberculin and brucellergen tests was negative.

To the intracutaneous toxoplasmin test, however, the response was strongly positive locally with a possible focal reaction as suggested by great improvement in the vitreous haze at the time of interpretation of the test 72 hours after it was made. The dye test gave positive results in a dilution of 1:512.

Treatment consisted of Daraprim and Combisul (3) orally, sodium Sulamyd drops, and sulfathiazole and neosporin ointments in the left eye, and iontophoresis with sodium Sulamyd solution 30 percent and streptomycin. The eye became quiescent within four weeks after therapy was instituted.

In July, one of the larger posterior lesions in the left eye became active, but quieted down promptly under the same regimen. At that time there was a positive reaction to the intracutaneous toxoplasmin test, and also to the dye test in a dilution of 1:256. The intracutaneous tuberculin and brucellergen tests gave negative results.

Late in August, the patient complained of blurring of the right eye. There was activation of an area to the lower temporal side with a considerable amount of vitreous exudates and a few keratic precipitates below in the cornea. At present this eye is responding well to treatment although some activity still remains.

COMMENT

This patient was a robust athlete showing no evidence of a diathesis suggesting a susceptibility to any disease. The suspicious factor in this case was the prolonged intravenous nutrient program necessary for the mother during pregnancy.

CASE 10

M. M., a white woman, aged 22 years, first consulted me in January, 1944, complaining of crusting of the eyelids. A seborrheic type of blepharitis was present, and there were indurated single heavily pigmented fundal scars in the lower temporal periphery of both eyes.

The patient was seen occasionally until August, 1955, when she complained of a stinging sensation and inflammation in the right eye. There were numerous vitreous opacities in this eye, and no active fundal lesion could be made out. In both eyes there were old heavily pigmented scars of retinochoroiditis in the temporal fundus fairly well out in the periphery. She was extremely nervous and losing weight. The intracutaneous tuberculin and brucellergen tests gave negative results, but the reaction to the intracutaneous toxoplasmin test was positive locally.

The area of skin testing except for the toxoplasmin control site became markedly erythematous two weeks after the tests had been made, particularly the site of the toxoplasmin test—a so-called Arthus phenomenon, according to Dr. Frank C. Metzger, the allergist consulted. The general physical examination was noncontributory except that the patient was greatly underweight. The blood picture was normal. Roentgen studies of the chest and skull gave negative evidence.

Daraprim and sulfadiazine were prescribed along with an antihistamine and sodium Sulamyd therapy locally in the eyes in drops and a sulfathiazole ointment. The ocular pattern improved rapidly in the right eye with clearing of the vitreous haze.

In December, response to the dye test was positive in a dilution of 1:32. In January and again in February, 1956, the reaction to the intracutaneous toxoplasmin test was positive. In July, the dye test gave a positive result in a dilution of 1:128.

Particularly notable, however, by this time was the change in the general condition with an increase in weight and improvement in some of the severe nervous symptoms. This change of course could have been coincidental and not the result of the therapy. The vision has remained unchanged throughout the whole course of treatment. It has always been as much as 20/20 in each eye.

CASE 11

O. C., a white woman, aged 70 years, whose vision had been failing for some time, particularly in the left eye, was first examined in April, 1955. She complained of black spots in front of both eyes.

Nuclear and postsubcapsular lens opacities were present in both eyes, and the thickened vitreous contained many coarse opacities. The vision corrected to 20/70 and 20/200 in the right and left eyes, respectively. A combined intracapsular extraction was performed on the left eye and one week later on the right eye.

As the reaction to the intracutaneous tuberculin and brucellergen tests was moderately positive two months later, Distrycin injections were given along with a tetracycline. The vision corrected only to 20/100 and 20/200. The vitreous was full of large opacities, but a suggestion of multiple chorioretinitic scars was observed in the right eye.

When the patient was next seen in April, 1956, the vision had deteriorated to 20/200 in the right eye and less than 20/400 in the left eye. The re-

action to the intracutaneous toxoplasmin test was strongly positive locally, and the result of the dye test was positive in a dilution of 1:64. Reaction to the intracutaneous tuberculin test was positive, but negative to the intracutaneous brucellergen test.

On Daraprim and Combisul (3) therapy plus Distrycin injections the ocular picture again began improving. Details of heavily pigmented multiple chorioretinitic lesions could soon be made out in both eyes through a less clouded vitreous, and after four months uninterrupted improvement continues, with the corrected vision now improved to 20/100 in the right eye and 20/200 in the left eye.

CASE 12

E. H., a white man, aged 33 years, in November, 1954, gave a history of blurred vision in the left eye for four months, during which time he had been under continuous treatment with no improvement. On examination, the right eye showed no abnormalities, and the vision of 20/25 corrected to 20/20+. In the left eye a few keratic precipitates of a quiet type were the only anterior changes noted.

In the fundus a large area of chorioretinitis with much pigment to the lower temporal side extended from the paramacular region fairly well out in the periphery. There was questionable activity, and the vitreous was filled with coarse opacities. Vision was not improved beyond 20/100 at distance and a J6 at near. Intraocular pressure was 22.3 mm. Hg (Schiøtz) in each eye. Intracutaneous tuberculin and brucellergen tests and the Kahn test gave negative results as did the physical examination and otolaryngologic and dental surveys.

A mixed staphylococcus-streptococcus vaccine was used for nonspecific desensitization. Paraaminosalicylic acid orally was prescribed and later oral Nydrazid and a tetracycline ointment locally with a cycloplegic every third day. The affected eye improved so much that by December vision was 20/20. Treatment was discontinued.

When the patient returned in July, 1955, the pathologic process in this eye again had become moderately active. The intracutaneous tuberculin test gave a negative result, and response to the intracutaneous brucellergen test was positive. The reaction to the intracutaneous toxoplasmin test was positive locally and to the dye test positive in a dilution of 1:126. Administration of Daraprim and Combisul (3) orally, sodium Sulamyd drops, and a sulfathiazole ointment resulted in rapid subsidence of the ocular activity.

In October there still was a local reaction to the intracutaneous toxoplasmin test, and another course of the same treatment for toxoplasmosis was prescribed. At that time the reaction to the intracutaneous brucellergen test again was positive, and negative to the intracutaneous tuberculin test.

In April, 1956, the vision in the involved eye was 20/20+, and the eye was quiet. All three intracutaneous tests gave negative results. Again in July the vision was the same in this eye.

COMMENT

It is noteworthy that the involved eye responded well to nonspecific desensitization with a staphylococcus-streptococcus vaccine and later to the accepted routine therapy for toxoplasmosis.

CASE 13

C. P., a white man, aged 38 years, first consulted me in May, 1953, complaining of total loss of vision in the left eye two years previously. He reported gradually failing vision and periodic attacks of uveitis in this eye since 1932, but the right eye functioned well. At the Cleveland Clinic the etiologic factor had been attributed to a latent brucellosis. A local ophthalmologist had advised enucleation of the eye.

In the right eye many large fundus scars of old chorioretinitis, heavily pigmented but quiescent, extended from near the macula above and also below. The vitreous was of unusually good structure. There was some peripheral field constriction for form and color. The vision easily corrected to 20/20+. The left eye was very soft; atrophy of the iris was present, and opacification of the lens was so great that no view of the fundus was obtainable.

General physical examination, including a roentgen study of the chest and skull and a dental survey, was noncontributory. Examination of the blood, which included an agglutination test for brucellosis, also gave negative results. Reaction to the intracutaneous tuberculin and brucellergen tests was negative.

The patient was seen periodically until March, 1956, when he reported noticing more spots before the right eye, a condition confirmed by ophthalmoscopic examination and also on slitlamp and Hruby lens observation. The intracutaneous tuberculin test and the intracutaneous brucellergen test gave negative results at that time. In the interim, the reaction to the former had been positive three times and negative once, and to the latter positive once and negative three times.

Reaction to the intracutaneous toxoplasmin test was strongly positive locally with some vesiculation, and there was a systemic reaction manifested by mild elevation of temperature and malaise. Reaction to the dye test was positive in a dilution of 1:64. A six-week course of Daraprim and sulfadiazine was prescribed along with sodium Sulamyd eyedrops and a sulfathiazole ointment.

The patient became so nervous under this medication that it was necessary to prescribe an Equanil tablet twice daily, but at no time was there bone marrow depression. At the end of this period the right eye was apparently quiescent. The left eye seemed to be unaltered. However, there is no light perception in this eye. During one episode, vision in the right eye was reduced to 20/30, but improved to 20/20.

COMMENT

It is of interest to note that at a prominent Northern ophthalmic clinic brucellosis was con-

sidered the etiologic factor in the uveitis in this case.

CASE 14

B. H., a white girl, aged eight years, complained in January, 1955, of loss of vision in the left eye, beginning about six months previously. In the right eye there was a high compound hyperopic astigmatic error with the vision correcting to 20/20—. Esotropia of about 30 prism diopters with hyperphoria was present in the left eye.

In the macular region there were a large chorioretinitic lesion with a considerable amount of pigment, and a smaller one between the nervehead and the macula. The vitreous contained a moderate number of opacities, but seemed of fair structure. An extremely high compound hyperopic astigmatic error was present in this eye with a corrected vision of 20/200—.

General physical examination, including roentgen studies of the skull and chest, and nose, throat, and dental surveys, was noncontributory. The intracutaneous tuberculin and brucellergen tests gave negative results. In March, reaction to the intracutaneous toxoplasmin test was strongly positive locally.

A recession of the internal rectus and inferior oblique muscles of the amblyopic left eye was performed with resultant fair parallelism of the globes. Under therapy with Daraprim and sulfadiazine orally and sodium Sulamyd eye drops and a sulfathiazole ointment, the left eye improved slightly with a corrected vision of 20/200+. A second intracutaneous toxoplasmin test in August gave negative results. In March, 1956, a third such test likewise gave negative results, as did the intracutaneous tuberculin and brucellergen tests. At that time blood was taken for the dye test, and the result was reported positive in a dilution of 1:16,384 by the South Bend Medical Foundation, which requested a résumé of the case.

COMMENT

In this case, the question arises as to whether or not the intracutaneous toxoplasmin tests performed 12 months and seven months before the blood was obtained for the dye test would have any effect on the titer. In Cases 1, 2, 3, and 8, also, skin testing with toxoplasmin antigen was performed months before the dye test was made.

DISCUSSION

Although not consisting of proved cases of ocular toxoplasmosis, this series represents cases in which this diagnosis is highly presumptive. Diagnostic criteria advocated by Woods and his co-workers[8, 15] were adhered to in these cases. The ocular picture conformed to the characteristic pattern, other systemic sources of uveitic infection were carefully sought, and a positive reaction to the intracutaneous toxoplasmin test and the Sabin-Feldman dye test was present in each case.

In two cases of the series the reaction to the dye test was positive in a titer of 1:32; in six, 1:64; in two, 1:126; in one, 1:128; in one, 1:256; in one, 1:512 and later 1:65,536; and in one, 1:16,384 (table 1). In five cases (1, 2, 3, 8, and 14) the controversial question could be raised regarding the possibility of skin testing causing an anamnestic rise in the dye titer, as Frenkel[17] contended, since the intracutaneous test had been performed at periods varying from seven months to more than a year prior to obtaining the blood specimen for the dye test in these cases.

In discussing this point with Dr. Ronald Wood and others in a position to have a competent opinion at the Wilmer Residents Meeting, I gained the impression that they regard it most unlikely that skin testing with toxoplasmin antigen has any bearing on the results of dye tests. At present, it appears that both the intracutaneous toxoplasmin test and dye test should be employed in a diagnostic study when ocular toxoplasmosis is suggested.

The role of the intracutaneous tuberculin and brucellergen tests in this unresolved problem is of course not to be ignored. The significance, if any, of the results of these tests in relation to toxoplasmosis remains problematic. In eight of the 14 cases of this series the intracutaneous tuberculin test gave a positive result. In six of the cases it was followed by a negative result at a later date, and in one case preceded by a negative result. Reaction to the intracutaneous brucellergen test was positive three times in one case and once in two cases (table 1).

Most of the cases in this series were characterized by an acute flare-up of the disease, particularly in the posterior portion of the uvea, superimposed on previously existing lesions. Case 1 illustrates the remarkable response to systemic antitoxo-

TABLE 1

TABULATION OF REACTIONS TO INTRACUTANEOUS TOXOPLASMIN, TUBERCULIN AND BRUCELLERGEN TESTS AND TO SABIN-FELDMAN DYE TEST

Case	Date of Test	Intracutaneous Toxoplasmin Test	Sabin-Feldman Dye Test	Intracutaneous Tuberculin Test	Intracutaneous Brucellergen Test
1	Sept. 49		N	P	N
	Dec. 50			N	N
	Jan. 55	P		N	N
	July 55	P			
	Aug. 55	P			
	Nov. 55		P 1:64		
	Jan. 56	P			
	Aug. 56	P			
2	March 55	N		N	P
	June 55			N	N
	March 56	P	P 1:32	N	P
	April 56	P		P	P
	July 56	P	P 1:256	N	N
3	Sept. 51			P	N
	Nov. 51			N	
	March 52			P	
	Sept. 52			N	
	Jan. 53			N	
	Sept. 53			N	N
	Feb. 54			N	N
	July 54			P	N
	Oct. 54			N	N
	March 55	N			
	Nov. 55	N		N	N
	Jan. 56	N			
	March 56	P	P 1:64		
4	March 56	P	P 1:128	P	P
	Aug. 56		P 1:256		
5	Feb. 56	P	P 1:64	N	N
	June 56	N	P 1:256		
	July 56	P		N	N
6	Oct. 50			P	N
	Sept. 55	P	P 1:126	N	N
	Nov. 55	P			
	Jan. 56	P		N	N
	Feb. 56		P 1:512		
7	May 41			P	N
	Nov. 49			P	N
	Dec. 49			P	P
	March 51			P	N
	Aug. 51			P	
	March 55	P	P 1:64	N	N
	April 56	P	P 1:32	P	P
8	Oct. 53	P	P 1:512		
	June 55	P		P	N
	March 56		P 1:65,536		
9	April 56	P	P 1:512	N	N
	July 56	P	P 1:256	N	N
10	Aug. 55	P		N	N
	Dec. 55		P 1:32		
	Jan. 56	P			
	Feb. 56	P			
	July 56		P 1:128		

(Continued on next page)

TABLE 1 (*Continued*)

Case	Date of Test	Intracutaneous Toxoplasmin Test	Sabin-Feldman Dye Test	Intracutaneous Tuberculin Test	Intracutaneous Brucellergen Test
11	June 55			P	P
	April 56	P	P 1:64	P	N
12	Nov. 54			N	N
	July 55	P	P 1:126	N	P
	Oct. 55	P		N	P
	April 56	N		N	N
13	May 53			N	N
	May 54			P	P
	June 54			N	N
	April 55	N		P	N
	Sept. 55			P	N
	March 56	P	P 1:64	N	N
14	Jan.55			N	N
	March 55	P			
	Aug. 55	N			
	March 56	N	P 1:16,384	N	N

TABLE 2

EVALUATION OF VISUAL RESULTS

Cases	Vision
1	Vision in right eye reduced to 20/50 during acute episode; returned to 20/30 with treatment. Complete recovery of central visual function.
2	Vision in left eye reduced to 20/40 during acute episode; improved to 20/20 with treatment.
3	Corrected vision of 20/50 in left eye improved to 20/20 corrected.
4	Vision of 6/200 in right eye improved after five months' treatment to 20/30 − 1.
5	Vision of 2/200 in the left eye improved to 20/200 after five months' treatment.
6	Treatment plus cataract extraction resulted in corrected vision of 20/40 minus in left eye with aphakic lens. At near, a J5 was obtained with presbyopic addition.
7	In 1941, corrected vision in involved right eye was 20/50 and in 1956 it was 20/30. In left eye, corrected distance vision was 20/30 in 1941 and also in 1956.
8	Patient too young for evaluation of visual function.
9	Vision in the left eye improved under treatment from 20/50 during an acute episode to 20/20.
10	No change. Vision in both eyes has remained at 20/20.
11	Vision improved from 20/200 and 20/400 to 20/100 and 20/200 in the right and left eye, respectively.
12	Vision in the left eye improved from 20/100 to 20/20.
13	Vision in the right eye improved from 20/30 to 20/20.
14	Vision of 20/200 unchanged, with definite central lesion and central scotoma present.

plasmosis therapy during an acute attack of uveitis, a result mentioned also by other authors, notably Cassady, Culbertson, and Bahler[11] and Ryan, Hart, Culligan, Gunkel, Jacobs and Cook.[20]

These authors warned particularly of objectionable side effects which may be experienced with the use of pyrimethamine in combination with sulfadiazine, adding that pyrimethamine should be used in humans only under close observation of the physician and with frequent laboratory checks until proved safe to use otherwise. Local therapeutic measures employed in this series included sodium Sulamyd solution (30 percent) sulfathiazole ointment, and iontophoresis with sodium Sulamyd and streptomycin.

In only one instance was it necessary to control associated mild bone marrow depression with oral folic acid therapy. Arrest of the infection, and in 11 of the 14 cases some improvement in vision, resulted from the treatment used. In a few instances, as in Cases 4, 5, and 6, the visual results were dramatic (table 2).

The practice of using Daraprim and sulfadiazine in presumptive cases of chorioretinitis apparently is becoming more general. Burnham and Beverman[21] reported a series of cases of presumptive toxoplasmic uveitis in which their excellent results with this therapy were basically similar to mine. They observed no severe toxic reactions from the use of these drugs, as was also my experience. A controlled clinical trial of Daraprim in cases of active uveitis led Perkins, Smith, and Schofield[22] to conclude:

"1. Daraprim had no detectable effect on the improvement of cases with a negative Toxoplasma reaction.

"2. Daraprim exerted a statistically significant effect on the improvement of cases having a positive Toxoplasma reaction.

"3. Toxoplasmosis was probably the cause of some 25 percent of the cases having a positive toxoplasmosis reaction.

"4. The best response was obtained in cases of circumscribed choroidoretinitis."

The first of these conclusions is not altogether in accord with my experience, but in others I readily concur.

The consensus seems to be emerging that smaller dosage over a longer period of time is as efficacious as more intensive treatment. Some authors advocated 25 mg. of Daraprim daily. Combisul (3) is tolerated better by some patients than sulfadiazine. The question of combining steroids with these drugs for minimizing the inflammatory reaction caused by the rupture of the pseudocysts is thought-provoking.

Treatment of this type, however, should not be instituted until tests have been employed to eliminate the more common diseases causing this condition. The lessened incidence of ocular tuberculosis and brucellosis should be a helpful diagnostic factor.

More widespread reporting of cases of chorioretinitic infection believed to be of toxoplasmic origin and more extensive research on the subject of ocular toxoplasmosis point the way to clarification of the diagnostic problem. The question of toxoplasmosis complicating the many ocular manifestations of prematurity may be more difficult to solve.

Conclusion

In his critical review, Sabin[10] aptly referred to "the interesting current dilemma regarding the nature, frequency, and "identification of postnatally acquired and adult ocular toxoplasmosis." Part of the dilemma is the growing interest on the part of practicing ophthalmologists in the relationship between Toxoplasma and uveitis.

The introduction of the dye test and at about the same time the skin test, which could be applied like the tuberculin test, brought a demand for serologic studies beyond the capacity of presently established laboratories to satisfy. Furthermore, the demand has preceded the acquisition of clearcut evidence as to the value of the immunologic tests in the diagnosis of ocular disease.[17] The knowledge of human toxoplasmosis has pro-

gressed stepwise since 1939, and its continued advance calls for concerted effort on the part of the research worker and the clinical ophthalmologist.

This presentation, with its discussion of the various aspects of the problem of ocular toxoplasmosis, particularly diagnosis, and a report of 14 cases believed to have a toxoplasmic etiology, is offered as a stimulus to the average clinical ophthalmologist to contribute his experience with cases of this type.

409 Citizens Building (2).

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THE EFFECT OF HYPOXIA ON THE HUMAN ELECTRORETINOGRAM*

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INTRODUCTION

Physiologic effects of reduced oxygen tension, or hypoxia, have been the subject of considerable research since the advent of high altitude flight.[1] The most widely investigated effects have been those which occur in relation to visual processes. Visual processes appear to afford an extremely sensitive index of hypoxia, and effects on these processes are obvious after an increase in altitude to 8,000 feet.[1,2]

Curves which relate such functions as visual acuity[3,4] and brightness discrimination[2,5] to the logarithm of luminance are reported to be shifted in the positive direction along the log luminance axis when oxygen tension is reduced.

Investigators have attempted to answer the question of whether rod and cone processes are equally affected by comparing the effects of hypoxia on psychophysical thresholds which are believed to represent cone function with the effects of hypoxia on thresholds which are believed to represent rod function. Some comparisons appear to indicate that rods and cones are equally affected.[2,6,7] Others indicate that rod functions are impaired more than cone functions;[8,9] still others indicate that cone functions are impaired more than rod functions.[10,11]

In an experiment in which they employed scotometric techniques to map visual fields under conditions of hypoxia at simulated altitude, W. Kyrieleis, A. Kyrieleis, and Siegert[12] found no changes in the sensitivity of the peripheral visual field. They concluded that effects reported by others were the manifestation of central nervous system effects which served to reduce "attention."

Investigators of the effects of hypoxia on visual function have expressed the belief that the visual impairment is neural and not photochemical.[2,7,8,13] Gellhorn and Hailman[1,14] have presented evidence which they interpret to indicate that the retinal synapses are the most probable seat of the impairment. Noell and Chinn[15,16] have measured electrical activity at various points in the mammalian visual system between the eye and the cortex during anoxia produced by breathing 100-percent nitrogen. They concluded that the cortex and geniculate body show the least resistance to anoxia, followed, in order of increasing resistance, by the retinal ganglion cells, the bipolar cells, and finally the photoreceptors.

The problem of studying effects of hypoxia is complicated by wide variation in breathing patterns of individuals suddenly exposed to a reduction of the oxygen tension in inspired air. Thresholds may either rise or fall, and upon resumption of breathing at normal oxygen tension they may rise again or fall from elevated to normal or even subnormal levels.[13]

In studying the effects of hypoxia on human vision, the electroretinogram (ERG) would seem to afford an excellent technique for investigating those effects which are restricted to the peripheral portions of the system. Since different portions of the electroretinogram wave are frequently associated with different functional elements in the eye, this technique may also afford further evidence as to the relative effects of hypoxia on rods and cones.[17–20]

Schubert and Bornschein[21] have found a slight reduction of b-wave amplitude of the electroretinogram and an increase in light detection threshold after the partial pressure of inspired oxygen is reduced to approxi-

* From the Aviation Medical Acceleration Laboratory, U. S. Naval Air Development Center. Opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or the endorsements of the Navy Department.

mately 42 mm. Hg. In one hemeralopic subject whose electroretinogram was described as having a clearly apparent x-wave no reduction of the x-wave amplitude was observed under hypoxia.

It would be desirable to compare the effects of hypoxia on components of the electroretinogram such as the a-wave, b-wave, and x-wave, all of which are elicited in the normal eye. These components can be stimulated selectively by the appropriate selection of the spectral distribution of the stimulating light. The purpose of the present experiment was to investigate the effects of hypoxia on these various components of the electroretinogram as measured in the normal human eye.

Apparatus

The light source which served as a photic stimulus was a General Radio, type 1532-B Strobolume. This device included a gas discharge tube which provided a very high luminance flash of short duration. No lens system was required for concentration of the light from this source. The discharge characteristic of the tube was sufficiently reliable so that no additional control of the flash presentation was necessary. No artificial pupil was used. The absence of either a pupil or lenses which require precise positioning of the eye made it possible for the eye to move laterally several millimeters with little or no change in the retinal illumination from a test flash. This latitude was considered desirable in an experiment involving hypoxia, effects of which might tend to reduce the precision of head positioning.

The Strobolume was operated at its high intensity setting. At this setting the gas tube was fired by the discharge of a 4.25-microfarad condenser which had been charged to 2,500 volts. Measurements were made of the temporal distribution of the energy emitted from the gas tube upon discharge in order to determine the reliability of this distribution. The energy was detected by a phototube, and the time characteristics of the flash were measured with reference to the calibrated sweep of an oscilloscope. Energy emitted from the Strobolume tube reached a maximum in approximately eight microseconds, decayed to 25 percent of maximum after 40 microseconds, and was reduced almost to zero after 80 microseconds. The decay was not completely smooth due to the inductive effect of the line which connected the condenser to the discharge tube. Photographs which were made of a large number of oscilloscope tracings indicated that there was almost no observable variability in the energy distribution when successive flashes were separated by intervals of a second or more.

The helical gas discharge tube of the Strobolume was mounted in a five-inch diameter reflector with a glass cover, the irregular inner surface of which served to diffuse the emitted light. This light source was fitted into a circular opening in the center of the large end of a truncated, pyramidal, wooden enclosure which extended into a copper-shielded, light-tight darkroom. A filter box was mounted on the small end of this enclosure inside the darkroom. The head of the subject was positioned by a chin rest and a rubber mouthpiece such that the right eye was located directly in front of the filter box. The distance of the eye from the light source was 25 inches, and the visual angle subtended by the source was approximately 11.5 degrees.

A small fixation light was located on the edge of the light source directly over its center. The brightness of this light could be adjusted from inside the darkroom. The area of the retina stimulated was an 11.5 degree circle directly above and bordering on the fovea. Test flashes were presented automatically at selected intervals by a synchronous motor-driven timing device which closed a microswitch.

In order to evoke components of the electroretinogram selectively, three different spectral distributions of the test light were employed. These are illustrated in Figure 1

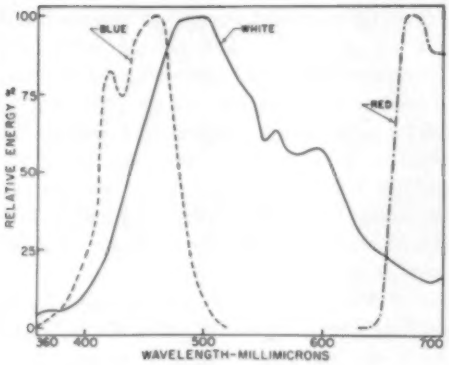

Fig. 1 (Brown, Hill, and Burke). Relative spectral energy distributions of three stimulus lights.

in terms of relative energy as a function of wavelength. The "white" distribution represents the spectral emission of the gas discharge tube unaltered by any selective filters, and is based on data provided by the General Radio Company. The "red" and "blue" distributions, respectively, were obtained by using a Corning 2030 red filter or a Corning 5543 blue filter with the white light source.

Luminance level of the test flashes was controlled by the use of Kodak Wratten neutral tint filters.

A platinum corneal electrode mounted in a plastic contact lens was used to record the electroretinogram. A fitted contact lens was made for the right eye of each subject.* A lead reference electrode was taped to the center of the forehead over a region to which electrode jelly had been liberally applied, and an indifferent electrode was attached to the left ear lobe to which electrode jelly had also been applied.

Recordings of the electroretinogram were made on a direct ink-writing, Grass 8-Channel electroencephalogram amplifier at a paper speed of 60 mm. per second. A reference point for the determination of latencies was provided by recording the output of a small photocell which was excited by the stimulus light.

The oxygen tension of inspired air was reduced by supplying appropriate mixtures of oxygen and nitrogen from pressure cylinders. These mixtures were delivered to the subject through a standard naval aviator's oxygen regulator. Valves were incorporated into the holder of the rubber breathing mouthpiece in order to minimize the volume in which CO_2 could accumulate. A nose clamp was worn in order to prevent dilution of the inspired gas by air in the darkroom.

Two oxygen and nitrogen mixtures were used. These contained either nine- or 15-percent oxygen, with the balance nitrogen. Equivalent altitudes were calculated for each of these mixtures with equations presented by Taylor.[22] It was assumed that pCO_2 remained constant at 39.9 mm. Hg and pH_2O was 47 mm. Hg. On this basis the oxygen tension of the nine-percent oxygen mixture at sea level is found to be approximately equivalent to the oxygen tension of normal air at 20,000 feet. The 15-percent oxygen mixture is equivalent to 8,200 feet of altitude.

Records of the rate and relative amplitude of respiration were obtained through the use of a pneumotachometer. This was located in the breathing tube which connected the oxygen regulator with the subject's mouthpiece. The signal from this device was demodulated and amplified by a Technitrol, C-R, Lilly Manometer. Breathing records were recorded on an Esterline-Angus Graphic Ammeter. These records were obtained in order to determine whether the responses of the two subjects to the reduced oxygen mixtures differed between subjects or from one session to another.

Procedure

A preliminary study was conducted in order to determine the relation of electroretinographic amplitude to stimulus intensity with each of the three spectral distributions.

Acknowledgment

* We wish to express our gratitude and appreciation to Mr. James MacMillan of the Bonschur and Holmes Optical Company for making the molds from which contact lenses were fashioned.

The subject was dark adapted for 30 minutes. Wratten neutral filters were used to vary intensity in 0.5-log-unit steps from a minimum value at which electroretinographic amplitude could not be measured up to the maximum intensity which could be obtained. Electroretinographic amplitude in log microvolts was plotted as a function of the density of neutral filters for the initial negative deflection and for the initial positive deflection with each of the three spectral distributions. Stimulus intensities were then arbitrarily selected for the three spectral distributions which resulted in an average positive deflection of approximately 100 microvolts. Under these conditions the amplitudes of the initial negative deflections were approximately 40 microvolts for red light, and 15 microvolts for blue and for white light. Peak amplitudes of the initial negative deflection were reached approximately 17 milliseconds after presentation of the stimulus with all three spectral distributions. Maximum amplitude of the positive deflection was reached after approximately 40 milliseconds with red light and after approximately 85 milliseconds with blue and with white light.

Two subjects were tested with the mixture containing nine-percent oxygen with each of the three spectral distributions at intensities which yielded a 100-microvolt positive deflection of the electroretinogram under normal conditions. The subjects were dark adapted for a minimum of 30 minutes at the beginning of each experimental session. Following dark adaptation, stimulus flashes were presented regularly at 30-second intervals for a period of 10 minutes, and the electroretinogram was recorded. During this period the breathing tube was disconnected from the regulator so that the subject was breathing room air. At the end of the 10-minute period the breathing tube was connected to the regulator and the subject commenced breathing the nine-percent oxygen mixture. Stimulus flashes were continued at the rate of one every 30 seconds. After an interval of 15 to 17 minutes the breathing tube was again disconnected and the subject resumed breathing room air. Electroretinographic recording was continued at the same rate for an additional 10 minutes or longer before terminating the session. Four sessions were conducted for subject J. B. and two for T. D. with the red stimulus. One session was conducted with the blue and one with the white stimulus for each of the subjects.

An additional session was conducted with each subject using the red stimulus light and with an oxygen-nitrogen mixture which contained 15-percent oxygen. The experimental procedure was otherwise identical with that outlined for the nine-percent oxygen mixture.

The presence or absence of an artificial pupil is reported not to affect the electrotinogram significantly.[23] However, reduced oxygen tension has been reported to affect both pupil size and the nature of the pupillary reflex.[24] It was therefore considered advisable to conduct an additional experimental session in which pupil size was controlled. Accordingly, the pupil of the right eye of subject J. B. was dilated by five applications of four drops of one-percent homatropine hydrobromide at 15-minute intervals. Following the final application the subject was dark adapted for approximately one hour, and then tested, as outlined above, with red light flashes. The nine-percent oxygen mixture was used for this procedure.

Results

The nature of the electroretinographic response under normal conditions has been briefly described in the preceding section. Typical responses to red, blue, and white stimulus lights are presented in Figure 2. Results obtained while the subject was breathing room air are shown in the column on the left. The greater initial negative deflection and the earlier rise to a positive maximum following stimulation with red light are clearly evident. The amplitudes of the positive deflection are approximately

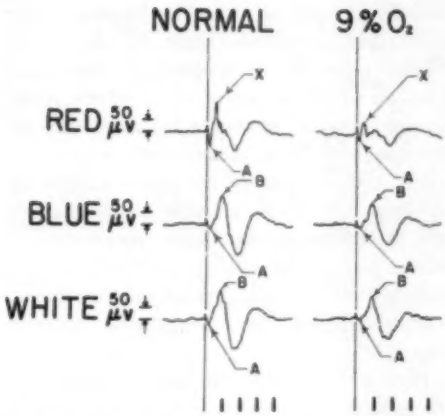

Fig. 2 (Brown, Hill, and Burke). Electroretinogram records obtained with each of three spectral distributions of the stimulus light. Records on the left were obtained while subject J. B. breathed normal air. Records on the right were obtained while subject J. B. breathed an oxygen-nitrogen mixture containing nine-percent oxygen.

100 microvolts for all three spectral distributions of the test light. Electroretinograms obtained after eight or more minutes of breathing the nine-percent oxygen mixture are presented in the column on the right of Figure 2. The amplitudes of the positive deflection appear to be reduced in all three cases, but it is evident that the extent of the reduction is greatest following stimulation by the red test light. No changes in the latencies of either the positive or the negative deflections were observed during hypoxia.

In the graphs at the top of Figure 3 the amplitudes of both the negative and the positive deflections are presented as a function of time during the experimental session for subject J. B. The negative deflection amplitudes are labelled "a-wave" for all three spectral distributions of the test light. The

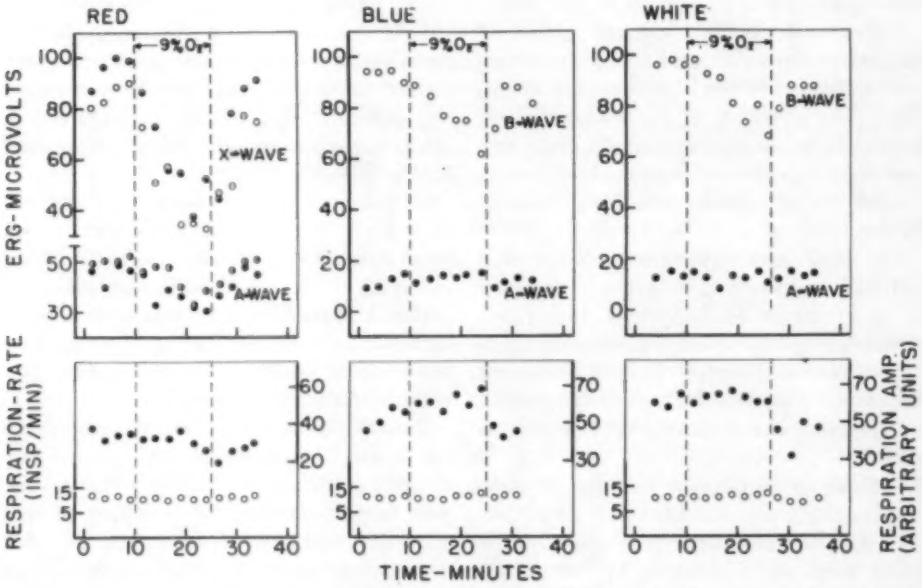

Fig. 3 (Brown, Hill, and Burke). Records of the amplitude of positive (x-wave and b-wave) and negative (a-wave) components of the electroretinogram during experimental sessions in which subject J. B. breathed an oxygen-nitrogen mixture containing nine-percent oxygen. Records are included for each of the three spectral distributions of the test light. Records of respiration frequency (open circles) and amplitude (solid circles) are presented below each of the records of electroretenographic amplitude. In the records for red light, half-filled circles represent one session; filled and open circles represent another session.

positive deflection amplitudes are labelled "x-wave" for red light and "b-wave" for blue and white light. Each of the plotted points represents an average of the amplitudes of five electroretinographic responses which were obtained at 30-second intervals over a period of two minutes. The interval during which the subject was breathing nine-percent oxygen is bounded by a pair of vertical dashed lines.

Amplitude of the x-wave begins to decrease almost immediately when the subject is switched from breathing room air to breathing nine-percent oxygen. This decrease in amplitude continues for at least six or seven minutes and amounts to more than 50 percent of the initial amplitude. When room air is again introduced after 15 or more minutes of breathing the nine-percent oxygen mixture, the amplitude of the x-wave increases up to a level near the initial level within six or seven minutes.

Two records obtained with red light stimulation have been presented in order to afford some indication of the reproducibility of the effect. The amplitude of the a-wave following red light stimulation shows a slight decrease during low-oxygen breathing but it is much less pronounced than the decrease of the x-wave.

The amplitudes of b-waves obtained with both blue and white light appear to decrease by about 20 or 30 microvolts during the period of breathing nine-percent oxygen. The a-wave amplitudes obtained following stimulation with blue and white lights show no significant change during the low-oxygen period.

Records of respiration rate and respiration amplitude are presented in Figure 3 below the electroretinographic records with which they are associated. The breathing records presented with the red light data were obtained during the session which is represented by the half-filled circles in the plot of electroretinographic amplitude. Breathing nine-percent oxygen does not appear to have much effect on these breathing records. There is some suggestion that respiration amplitude may be decreased slightly upon the resumption of breathing room air after the period of breathing nine-percent oxygen. It should be noted that no effort was made to calibrate the respiration recordings in terms of the actual volume of air inspired. These records were obtained only in order to detect changes in respiration within any given run as a result of administration of the low-oxygen mixture. Amplitudes are not comparable between runs.

Figure 4 presents the same information for subject T. D. as that which is presented in Figure 3 for J. B. An extensive decrease in x-wave amplitude during nine-percent oxygen breathing is evident, although recovery following the resumption of breathing normal air occurs to a lesser extent than in the case of J. B. The a-wave amplitude after red light stimulation also appears to show a decrement during hypoxia. The hypoxia induced by breathing nine-percent oxygen did not have any consistent effect on the amplitude of either the a-waves or the b-waves following stimulation with blue light or with white light.

Breathing records obtained for T. D. are quite irregular, but there does seem to be some indication of a reduction in amplitude following the return to normal air after the period of breathing a nine-percent oxygen mixture. In addition, there is an apparent reduction in respiration rate which occurs with the return to room air.

Results obtained with the 15-percent oxygen mixture are presented in Figure 5 for subjects J. B. and T. D. The red test light was used to investigate the effect of this condition because red light had afforded the most sensitive indication of the effects of breathing the nine-percent oxygen mixture. With the exception of the higher oxygen tension, all conditions were the same as those which prevailed in obtaining the data presented in Figures 3 and 4. The effect on electroretinographic amplitude at

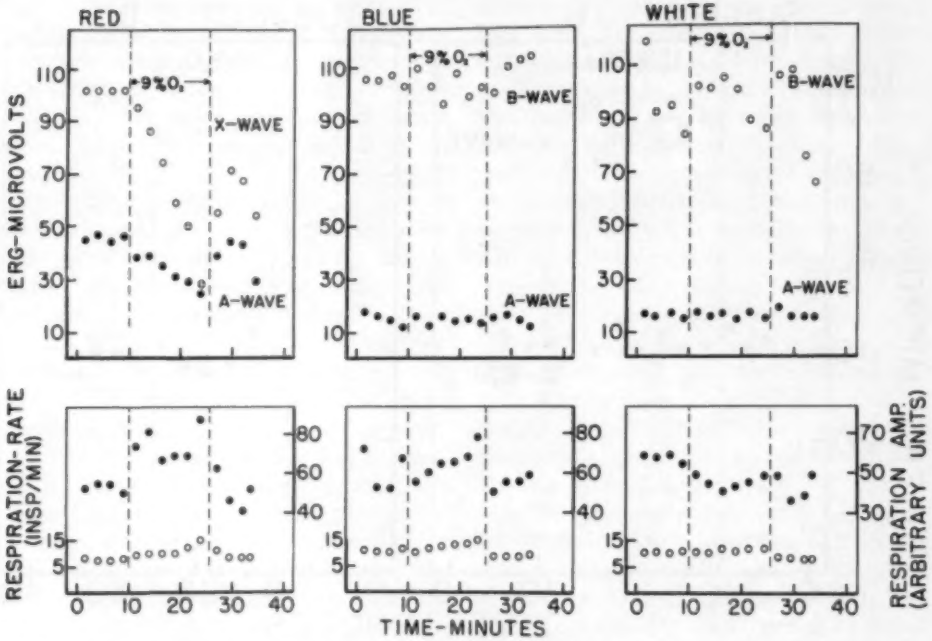

Fig. 4 (Brown, Hill, and Burke). Records of the amplitude of positive (x-wave and b-wave) and negative (a-wave) components of the electroretinogram during experimental sessions in which subject T. D. breathed an oxygen-nitrogen mixture containing nine-percent oxygen. Records are included for each of the three spectral distributions of the test light. Records of respiration frequency (open circles) and amplitude (solid circles) are presented below each of the records of electroretinographic amplitude.

this level of oxygen reduction is not clear-cut. There is some suggestion of a decrease in x-wave amplitude but the decrease is small, if significant.

Results obtained with subject J. B. after dilation of his pupil with homatropine were very similar to the results obtained in the normal eye. Average amplitude of the positive x-wave following red light stimulation was a little over 100 microvolts when the subject breathed room air. During the period of nine-percent oxygen breathing the amplitude reduced to about 40 microvolts. A-wave amplitude was approximately 50 microvolts during room-air breathing. This amplitude reduced to about 30 microvolts and showed increased variability during the nine-percent oxygen period. These results may be compared with results presented in Figure 3 for red light. Amplitudes are slightly greater when the pupil is artificially dilated, but the extent of the reduction is almost identical with that observed in the normal eye.

Discussion

It seems clear from the results of the present experiment that hypoxia induced by breathing nine-percent oxygen has an effect on the electroretinogram which is specific to the x-wave response following stimulation with red light. This is in marked contrast to the result reported by Schubert and Bornschein[21] for their hemeralopic subject. The "clearly apparent x-wave" of the hemeralope showed no reduction under hypoxia. It is possible that the "x-wave" observed in the hemeralopic eye after stimulation with white light does not represent the same process as the "x-wave" observed in the normal eye after stimulation with red light.

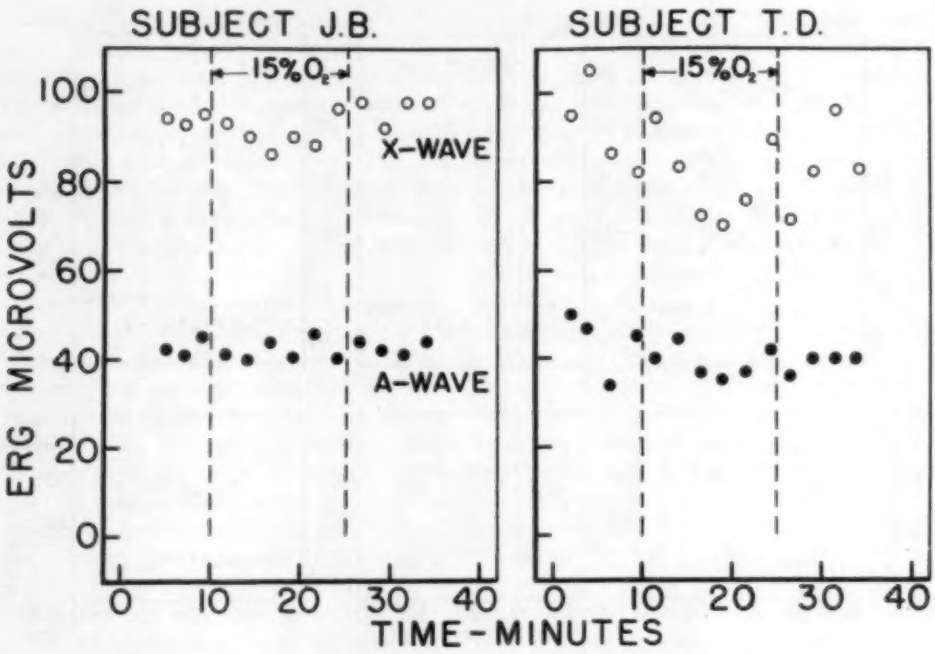

Fig. 5 (Brown, Hill, and Burke). Records of the amplitude of the positive (x-wave) and negative (a-wave) components of the electroretinographic response to red light during experimental sessions in which subjects breathed 15 percent oxygen. (Subjects J. B. and T. D.)

The facts that the x-wave is evoked in the normal eye by red light and that it is less subject to diminution of amplitude at higher levels of light adaptation than is the b-wave[18] have led several investigators to associate x-wave with cone function.[17–20] Schubert and Bornschein[19] and Armington[20] have reported that no x-wave can be evoked by red light stimulation in the protanopic, or red-blind eye. This latter finding has led to the suggestion that the x-wave is an index of the function of a specific kind of cone, a red receptor.

It is possible that the x-wave occurs with cone activity of any kind but that it is usually obscured by the positive wave which represents rod activity. When red light is used, the relative stimulation of the rods may be sufficiently reduced so that the x-wave is revealed. If the x-wave does represent cone activity in general, then it may be of the same origin as the fast positive wave which is observed following stimulation with a flickering light of high intensity.[17] It would therefore be of interest to determine the effects of hypoxia on the fast positive wave evoked by a white flickering stimulus of high intensity. A reduction of amplitude comparable to that which we observed with red light would constitute evidence for such a common origin.

A possible interpretation of the results of our experiment is that the metabolic processes which maintain the sensitivity of cones (or perhaps, more specifically, the red receptors) are highly oxygen-dependent. There is an indication in Figures 3 and 4 that recovery of x-wave amplitude is not complete after the subject has breathed normal air for 10 minutes following the period of breathing the nine-percent oxygen mixture. This delay may reflect the gradual regeneration of some critical component that is maintained as a result of oxygen metabolism.

The idea that our results mirror the effect of hypoxia on a cone process, perhaps even a specific color receptor, is an appealing one. However, there is at least one other possibility. The decreased x-wave amplitude which we observed may not be directly related to changes in the receptors at all. It may simply reflect a change in spectral transmission of the medium through which light must travel before it reaches the receptors. For example, before reaching the receptors, light must pass through a layer of the retina approximately 0.3 mm. in thickness which contains many blood vessels.[25] It is known that the vessels dilate during hypoxia,[26] that there is increased hemoglobin in circulation, and that the oxygen saturation of the blood is reduced.[27] The spectral transmission of reduced hemoglobin is lower than that of oxyhemoglobin for light which has a spectral distribution like that of the red light used in this experiment.[28] If there is relatively more reduced hemoglobin, and a greater absolute amount of blood through which the light must pass during hypoxia, the result might be a reduction in x-wave amplitude during hypoxia.

In order to test this hypothesis, the following procedure was employed. Two samples of oxyhemoglobin solution were prepared which had been diluted to approximately one-twentieth the concentration of human blood. These samples were contained in quartz cells which could be mounted in the eyepiece of the apparatus and which were sufficiently large that they did not in any way restrict the subject's view of the stimulating light. The thickness of the sample of solution through which light had to travel to reach the eye was 1.0 cm. With the hemoglobin in solution diluted 20 to 1 as compared to whole blood, the 1.0-cm. sample thickness may be considered as approximately equivalent to a 0.5-mm. thickness of whole blood.

The electroretinographic response of subject J. B. was recorded following stimulation through the red Corning 2030 filter and through each of the samples of oxyhemoglobin. The electroretinographic response was found to be almost identical in form and amplitude with each of the two samples. The oxyhemoglobin in one of the quartz cells was then completely reduced by the addition of a measured amount of sodium hydrosulfite. The electroretinographic measurements were then repeated, alternating between the cell which contained oxyhemoglobin and that which contained reduced hemoglobin. The electroretinographic x-wave amplitude following stimulation through the oxyhemoglobin sample remained at the level which had been measured initially, 42 microvolts. The electroretinographic x-wave amplitude following stimulation through the sample of reduced hemoglobin was reduced to 31 microvolts.

In the preliminary study mentioned above we determined the relation between electroretinographic amplitude and stimulus intensity. From the results of this study it was possible to estimate the reduction of intensity of the red test light which would result in a reduction of x-wave amplitude from 42 to 31 microvolts. The required reduction is equivalent to an increase in density of 0.19. A density increase of approximately 0.60 would be required for the same reduction of x-wave amplitude as that which was measured during hypoxia resulting from breathing nine-percent oxygen.

The amount of hemoglobin in our sample was much greater than that through which light must travel in the eye, and the reduction of oxyhemoglobin in our sample was much more nearly complete than the reduction of hemoglobin in the blood during hypoxia. We therefore conclude that x-wave amplitude reduction observed during hypoxia is only partially the result of a filtering effect of hemoglobin in the blood.

Although some other substance may have a selective filtering effect on red light during hypoxia, it is possible that the reduction of x-wave amplitude during hypoxia may reflect a direct effect on a specific kind of receptor. In view of the lack of consistency of results which have been reported

for psychophysical studies of the relative effects of hypoxia on rod and cone thresholds, it would seem desirable to conduct further investigations of psychophysical thresholds which require rod function and cone function using a variety of spectral distributions of the test light. Hypoxia may prove a useful device for studying the relation of the x-wave of the electroretinogram to some psychophysical function of vision.

Summary

Hypoxia was induced in two subjects by having them breathe, at atmospheric pressure, oxygen-nitrogen mixtures which contained lower percentages of oxygen than that found in normal air. The amplitude of the electroretinographic response to stimulation by red light was reduced by more than 50 percent while subjects breathed a mixture containing nine-percent oxygen. This mixture is equivalent to the atmosphere at an altitude of 20,000 feet. Implications of this finding are discussed in relation to current interpretations of the electroretinogram.

Medical Acceleration Laboratory.

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A SIMPLE OPERATION FOR SENILE SPASTIC ENTROPION*

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Almost any procedure which is capable of tightening the orbicularis oculi muscle is able to cure spastic senile entropion. Among the methods used are cauterization, excision of tissue, and plastic procedures. Some are more difficult than others, some achieve better results.

In 1878, M. Cusco[1] successfully treated spastic entropion by "deep cauterization, drawing the platinum needle across the skin." He was probably the first in modern times to use cauterization for entropion. Terrien,[2] in 1902, used cautery of the skin and muscle extensively for this condition—varying its depth with the severity of the deformity. In America, Ziegler[3] popularized cauterization by describing his thermo-puncture technique. Apparently cautery is effective by causing a shrinkage and scar retraction of the orbicularis oculi. This in turn pulls the inverted lid outward.

Many other procedures have been devised to accomplish the same purpose. Thus, the Celsus operation[4] removes a block of skin and orbicularis to shorten the skin surface of the lid. Vialeix,[5] in 1929, combined an excision of the marginal orbicularis fibers with deep cautery of the tarsus. An extensive excision of orbicularis muscle from the lid and orbital areas was described as effective by Kettesey[6] in 1948.

Among plastic procedures, those of Wheeler[7] are outstanding. His operations consist mainly of overlapping strips of orbicularis. A similar technique, involving torsion of the orbicularis, was described by Strampelli.[8] Kirby[9] described a procedure which tightens the orbicularis by pulling a strip of the muscle laterally. The same author[9] describes many other forms of treatment of spastic entropion in his review of the literature which need not be duplicated in this presentation.

During a visit to Paris in 1952, I was permitted to attend the Quinze-Vingts Eye Hospital. While there, I saw the eye surgeons perform an extremely simple operation for senile entropion. Not only was the operation simple to perform but I was told that the results were uniformly good. Upon my return to New York, I could find no description of this procedure in the literature. The Armed Forces Library researchers likewise were unable to locate such a description. During the next three years, I had the opportunity of using this procedure, slightly modified, on 10 cases. The French surgeons had been right. The operation was simple and the results, for the most part, excellent. For these reasons, I felt that the procedure should be in the literature so

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Fig. 1 (Bodian). Dotted line indicates skin incision for repair of spastic entropion. Procaine is injected along this route, beginning slightly lateral to outer canthus. Entropion and trichiasis are evident.

that others might assay its advantages and possible pitfalls.

Operative procedure

The description to follow is the technique which I have used. It differs from the French method only in the varied types of coagulation, the use of the Erhardt clamp, and in the use of catgut sutures (figs. 1 through 6).

The patient is given an appropriate preoperative sedative to allay apprehension. For anesthesia, several drops of pontocaine (one

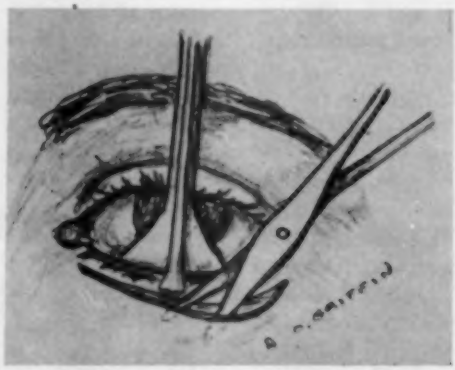

Fig. 2 (Bodian). The lower margin of the skin incision is undermined downward for about eight mm., separating the skin from the underlying orbicularis oculi. The Erhardt clamp is in place.

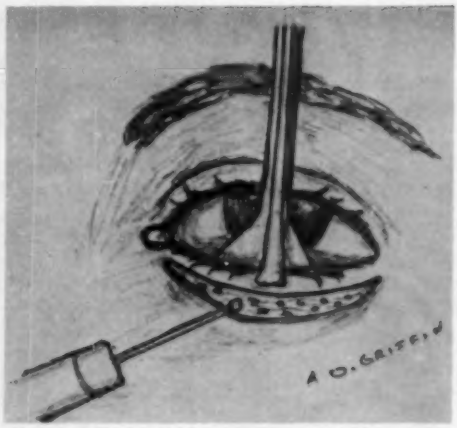

Fig. 3 (Bodian). The exposed orbicularis oculi is being coagulated with a two-mm. ballpoint diathermy electrode in two parallel rows.

percent) are instilled into the conjunctival sac and two percent procaine solution containing 1:100,000 epinephrine is injected subcutaneously. For the latter, a three-cm. 23-gauge needle is introduced into the skin five mm. below the lid margin and five mm. lateral to the external canthus. As the skin is ballooned out with solution, the needle traverses the subcutaneous space medially until the entire lower lid has been infiltrated. This may require two to three cc. of anesthetic solution. Pressure helps disperse the procaine. An Erhardt clamp is applied to the lower lid.

The skin incision is parallel to the lid margin, two to three mm. below it, and runs the entire length of the lid. A No.-15 Bard-Parker scalpel is quite satisfactory. The lower skin edge is undermined with a Stevens scissors for eight mm. along its entire length, separating it from the underlying orbicularis oculi. When bleeding has been controlled, the orbicularis is coagulated by any one of several means. A ballpoint diathermy electrode, a hot muscle hook, or the Hyfrecator* may be used.

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* Made by the Birtcher Corporation, Los Angeles 32, California.

Two parallel rows of coagulations are made. These are two and five mm., respectively, below the line of incision. The coagulations just about touch each other and vary in intensity with the severity of the entropion. Because of ease of manipulation, diathermy is the modality of choice. If diathermy is not available, the same result can be accomplished with a red hot muscle hook (Case 4) or the Hyfrecator (Cases 2, 3, and 5) applied to the orbicularis oculi in the same manner.

A strip of skin is now excised from the lower wound edge measuring three to four mm. in width and extending the length of the original incision (approximately 30 mm.). The skin is closed with interrupted plain 4-0 catgut sutures and an antibiotic ointment is applied. A semipressure bandage covers the wound and the patient leaves the operating room in a wheel chair.

The first dressing is done in 24 to 48 hours, when a small gauze patch with antiseptic ointment is applied to the wound. This is changed daily. Since the great majority of these patients are aged, they are permitted out of bed immediately. The use of plain catgut sutures obviates the need for their removal. In the aged, the less we manipulate, the happier is everyone concerned. The skin patch is discarded in about a week.

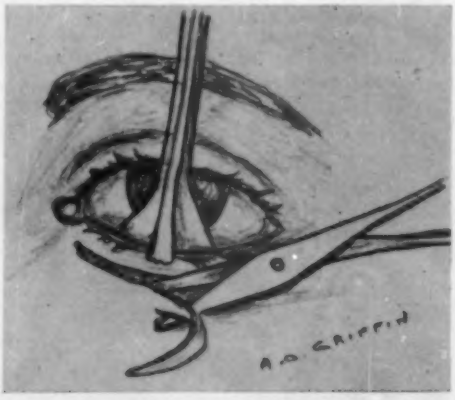

Fig. 4 (Bodian). An elliptical strip of skin, three to four mm. wide, is excised along the lower margin of the skin incision.

Fig. 5 (Bodian). The skin is closed with several interrupted 4-0 plain catgut sutures.

Results

In 10 cases operated upon for senile entropion, using the above technique, the results have been excellent. The lids no longer turned in to produce an irritating, infective trichiasis. The cases have been followed from six to 33 months. One patient (Case 6) has had a slight overcorrection resulting in a mild ectropion. However, this has been asymptomatic and certainly preferred to her previous condition. Six cases were treated with diathermy, three with Hyfrecator, and one with thermal coagulation. Because of the wrinkled skin, it is almost impossible to see

Fig. 6 (Bodian). The operation is completed. An antibiotic ointment and a semipressure patch are applied to the eye. There should be no entropion evident at this stage.

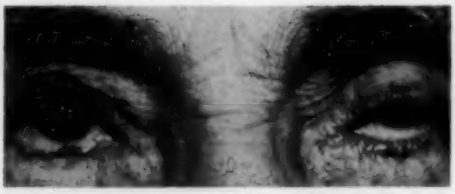

Fig. 7 (Bodian). Case 1, R. C., right eye shows marked spastic entropion.

Fig. 8 (Bodian). Case 1, R. C., 33 months after surgery for spastic entropion.

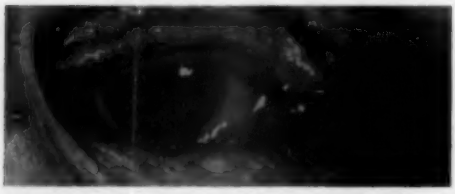

Fig. 9 (Bodian). Case 2, F. B., preoperative appearance.

Fig. 10 (Bodian). Case 2, F. B., 26 months postoperative.

the skin incision after two to three weeks. The results in all were gratifying.

Case reports

Case 1 (figs. 7 and 8)

R. C., a 76-year-old white housewife, had been complaining of tearing, redness, pain, and the feeling of a foreign body in her right eye for a period of 14 months. This had had a spontaneous onset and had grown worse. Her previous ocular history included bilateral combined cataract extractions two and seven years prior to the onset of the present condition.

The entropion was operated upon on June 20, 1953, at the Jewish Hospital of Brooklyn. The operative procedure already described was followed. The orbicularis oculi was coagulated with a two-mm. ballpoint diathermy electrode in the manner described. Healing was uneventful. The end-result has remained functionally and cosmetically excellent for the past 33 months.

Case 2 (figs. 9 and 10)

F. B., an 82-year-old white housewife, had been complaining loudly for eight months of irritative symptoms in her right eye as a result of spastic entropion. She had been in the Hebrew Home and Hospital for the Aged for the past six years. Her general condition included arteriosclerotic cardiovascular disease and cerebral arteriosclerosis. On January 20, 1954, she was operated upon. Because the diathermy apparatus was not available, the orbicularis oculi muscle was coagulated by means of the Hyfrecator. The current was applied to the muscle until it turned a greenish-brown color. The remainder of the operation was as already presented. Healing was painless. For 26 months since then, the patient has been comfortable, the eye has been white, and the cosmetic result has been excellent.

Case 3 (figs. 11 and 12)

H. F., a 78-year-old white man, a retired tailor, complained of a severe scratching sensation in his right eye. In addition, there was much tearing, redness, and exudation of thick yellow pus. He had a typical senile spastic entropion. He had been at the Brooklyn Hebrew Home and Hospital for the Aged for the past eight years and suffered from generalized arteriosclerosis. His eye was operated upon on June 7, 1954, with the technique described using the Hyfrecator as in Case 2. With antiseptic drops the eye soon became clear, free of pus, and completely asymptomatic, in which condition it has remained for the past 21 months.

Fig. 11 (Bodian). Case 3, H. F., preoperative.

Fig. 12 (Bodian). Case 3, H. F., 21 months postoperative.

CASE 4

B. C., a 77-year-old white housewife, complained of soreness, tearing, redness, and pus in her right eye. The right eye had the classical picture of senile spastic entropion. Bilateral cataracts had reduced her corrected vision to, O.D., 20/200; O.S., 20/70. Her general condition included moderate obesity and vascular hypertension. Because of local symptoms and because cataract surgery was deemed necessary, it was considered important that the entropion first be corrected. On September 2, 1954, the patient was operated upon at the Brooklyn Eye and Ear Hospital (service of Dr. Walter V. Moore).* The orbicularis oculi muscle was coagulated to a green-brown color in two parallel lines by means of a red-hot muscle hook. The remainder of the procedure was similar to that already described. For the past 18 months, the results have been most gratifying from a functional and cosmetic standpoint. The patient is to return for cataract surgery.

CASE 5 (figs. 13 and 14)

S. W., an 82-year-old white former housewife, had been complaining of smarting, redness, and tearing from her left eye, for the past three years. Examination showed a typical senile spastic entropion. For the past 12 years, she had been at the Brooklyn Hebrew Home and Hospital for the Aged where a diagnosis of generalized arteriosclerosis and arteriosclerotic heart disease had been made. On October 25, 1954, the eye was operated on using the Hyfrecator as in Cases 2 and 3. Healing was uneventful. The patient's eye has been asymptomatic since the operation 17 months ago.

CASE 6 (figs. 15 and 16)

S. P., a 68-year-old white housewife, complained of a foreign-body sensation in her right eye as well as redness, tearing, and pain. Her right lower lid had a typical senile spastic entropion which had caused a moderately severe keratoconjunctivitis. She had been at the Brooklyn Hebrew Home and Hospital for the Aged for three years. Her general condition included mild, controlled diabetes mellitus and generalized arteriosclerosis. The lower lid was operated upon on February 7, 1955, using a two-mm. ballpoint diathermy electrode as the coagulating agent. This case healed with a slight overcorrection. The

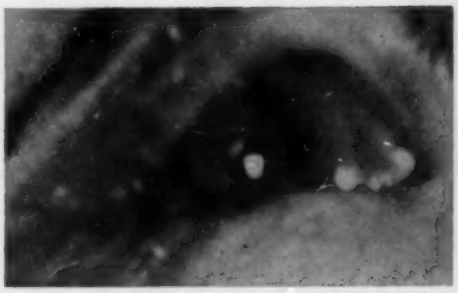

Fig. 13 (Bodian). Case 5, S. W., preoperative.

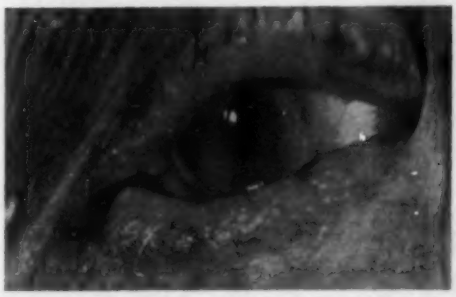

Fig. 14 (Bodian). Case 5, S. W., 17 months postoperative.

Fig. 15 (Bodian). Case 6, S. P., preoperative.

*All service cases done at Brooklyn Eye and Ear Hospital were done from the service of Dr. Walter V. Moore who kindly granted permission to report them in this article.

Fig. 16 (Bodian). Case 6, S. P., 13 months postoperative. Note the slight ectropion.

cornea soon cleared with antiseptic ointments. All signs and symptoms relative to the entropion have been absent. The slight resultant ectropion (fig. 16) has caused no difficulty. For 13 months postoperatively, the patient has had no eye complaints.

CASE 7

A. K., an 80-year-old white housewife, complained of sticking pain, redness, tearing, and purulent discharge from her right eye for the previous eight months. Examination showed her to have a spastic entropion and secondary purulent keratoconjunctivitis. Her general condition included hypertensive and arteriosclerotic heart disease. She had been in the Brooklyn Hebrew Home and Hospital for the Aged for the previous six years. On April 1, 1955, the entropion of the right eye was repaired at the same hospital, with the use of ballpoint diathermy. The immediate reaction was mild swelling of the lower lid. An 11 months' follow-up showed an excellent functional and cosmetic result.

CASE 8

C. C., a 70-year-old retired cobbler, appeared at the Brooklyn Eye and Ear Hospital Eye Clinic with signs and symptoms of right senile cataract and flaccid (senile) ectropion of the right lower lid. On March 17, 1955, a combined intracapsular cataract extraction was done on this eye which yielded 20/30 corrected vision. On May 26, 1955, a Kuhnt-Szymanowski repair of the ectropion resulted in an overcorrection which had all the signs and symptoms of a spastic senile entropion. Because of the severe irritation resulting from this condition, the entropion was operated upon on August 11, 1955, using ballpoint diathermy. The result has been functionally and cosmetically excellent over a seven months' period.

CASE 9

M. R., a 51-year-old carpenter had a combined intracapsular cataract extraction on June 30, 1955, at the Brooklyn Eye and Ear Hospital. Convalescence was complicated by the presence of a typical spastic entropion of the right lower lid. On August 25, 1955, this lid was operated upon using the ballpoint diathermy. Within a week, the eye became white and quiet on local medication which had been ineffectual in the presence of the entropion. Vision became correctible to 20/20 and the lid has had excellent function and appearance for the past seven months.

CASE 10

G. R., a 53-year-old milk-delivery man, appeared at my office with signs and symptoms of spastic entropion of the right lower lid, as well as xanthelasmas of all four lids. On September 13, 1955, the xanthelasmas were excised and the right lower lid was operated upon for the entropion, using a ballpoint diathermy. For six months there has been an excellent functional and cosmetic result.

DISCUSSION

It is admitted that the series of cases herein reported is rather limited and some of the follow-up periods are brief. However, since the results were so uniformly satisfactory, I felt that it would not be amiss to publish them so that others might try this same procedure.

Its simplicity is such that no plastic surgical techniques are necessary, which, aside from their technical difficulty, occasionally are doomed to failure because they depend on sutures which may slip or cut through tissue. The procedure described does not depend on sutures for its success. The occasional operator will, I think, find this procedure of great value.

It will be noted that the manner of coagulation of the orbicularis oculi muscle may be varied. In one case, a hot muscle hook was used, in three cases the Birtcher Hyfrecator, and in six cases ballpoint diathermy. This again emphasizes the primary principle of this operation, namely, coagulation of the orbicularis oculi muscle which results in scar formation and shrinkage.

To be sure, this operation is a somewhat more complicated one than Ziegler cautery punctures but also, I believe, it is a more dependable procedure. Very often, the senile patient does not permit the surgeon to operate a second time for the same condition. It

TABLE 1

SUMMARY OF CASES OPERATED ON FOR SPASTIC ENTROPION

Case	Sex	Age (yr.)	Date of Operation	Modality	Result	Length of Follow-up (mo.)
1	F	76	6/20/53	Diathermy	Excellent	33
2	F	82	1/20/54	Hyfrecator	Excellent	26
3	M	78	6/ 7/54	Hyfrecator	Excellent	21
4	F	77	9/ 2/54	Hot muscle hook	Excellent	18
5	F	82	10/25/54	Hyfrecator	Excellent	17
6	F	68	2/ 7/55	Diathermy	Slight over-correction	13
7	F	80	4/ 1/55	Diathermy	Excellent	11
8	M	70	8/11/55	Diathermy	Excellent	7
9	M	51	8/25/55	Diathermy	Excellent	7
10	M	52	9/13/55	Diathermy	Excellent	6

is my opinion that the operation described here practically never requires a second operation. This opinion is based not only on my own experience but also on the reports given to me by the French surgeons whom I first saw perform it.

SUMMARY AND CONCLUSION

An operation to correct senile spastic entropion is described. The technique is simple and the results highly gratifying. Case reports on 10 patients who have had this operation indicate uniform success. The procedure can be done by the occasional operator with little difficulty. Experienced assistance is not necessary. I would appreciate further reports on this procedure to evaluate its efficacy more completely.

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EXPERIMENTAL SECONDARY EFFECTS OF TOPICAL ANESTHESIA OF THE CORNEA*

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In former experiments,[1] I showed that the continued topical application of solutions of the usual anesthetics causes, in addition to the appearance of lesions, a gradual loss of the anesthetic power of these drugs which, after some time of continual administration, vanishes completely. After this loss of effect of the anesthetic, there was first a period in which the cornea was sensitive to touch, but not anesthetizable; afterward the whole or some parts grew insensitive. More or less extended erosions were found. The doubt arose whether these effects were really caused by the anesthesia itself, or by a dehydrating secondary effect produced either by the anesthetic drug or by physical dehydration of the cornea due to improper blinking.

To resolve this doubt I performed a series of experiments, using the same anesthetic drugs used in the former experiments, in the same concentration but in an ointment.

EXPERIMENTS

The method of the experiments was the same as that used in the solution ones. The cornea of one of the eyes of adult rabbits not previously used for experimental purposes was anesthetized by application of an ointment of the anesthetic drug. Application was repeated each time the anesthesic effect was gone. The cornea was considered anesthetized whenever the corneopalpebral reflex, elicited by touching the cornea with a wisp of cotton, was absent. The cornea was considered not anesthetized when it began to heal. With this criterion the aspect only is considered and not depth or degree of anesthesia. When the experiment extended over more than one day, I worked eight hours each day.

I used a vaseline ointment (it was necessary to include 10 percent lanolin in order to assure a proper uniform distribution in the Nupercaine ointment), applying with a glass applicator 65 ± 15 mg. of the ointment under the upper lid. This measure proved to be of no importance because the rabbit squeezed out most of the applied ointment, which was wiped away in order to prevent a further accidental application of the ointment hanging on the lids.

After a more or less prolonged period of this continued application, the anesthetic lost its effect. I considered the anesthetic without effect when the application of the ointment failed to stop the corneopalpebral reflex over a period of at least 15 minutes (usually it stops in at most 30 seconds).

After this failing of the anesthetic power, there was a period in which the cornea was sensitive (presence of the reflex) but not anesthetizable; afterward the sensitivity vanished over at least part of the cornea. At the same time there was a constant finding of more or less extended erosions. The erosions were verified by staining with one-percent fluorescein solution; the insensitive areas were checked by touching them with a wisp of cotton. In further descriptions these areas are measured in fractions of the whole extent of the cornea. Each rabbit was observed for a week to check the evolution of the insensitive and eroded areas.

Four rabbits were used for each anesthetic ointment studied:

A. *Two-percent Neotutocaine ointment.* The time of action of each anesthetic application was on a whole greater than with the

* This work was done in the Scientific Section of the Geyer Laboratories with rabbits from the Institute of Veterinary Research of Rio Grande do Sul. I am greatly indebted to the directors of these two institutions. I wish also to express my thanks to the Pharmacology Department of the Medical School of Pôrto Alegre for the cocaine, the Bayer Laboratory for the Neotutocaine, and the Ciba Laboratory for the Nupercaine.

solution. This was observed with all the anesthetics used. I suppose that it is due to the more prolonged contact. The period of anesthesia did not drop off gradually, as with the drops, but vanished rather suddenly. The results with the four rabbits of the series showed:

1. In the eight hours of the first day 16 applications of the ointment were made; on the second day four applications during one hour and 24 minutes. The anesthetic then lost its effect. The rabbit showed an erosion of the whole cornea which afterward grew insensitive. After one week, the cornea had healed to one-tenth its extent and the insensitive area had been reduced to two-thirds, and included the erosion.

2. In the eight hours of the first day the ointment was applied 16 times; on the second day seven times during two hours and 21 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of the whole cornea which afterward became insensitive. After one week, it had healed to one-ninth and the insensitive area had been reduced to one-third and included the erosion.

3. In the eight hours of the first day the ointment was applied 12 times; on the second day four times in two hours and 50 minutes when the anesthetic lost its effect. The rabbit showed an erosion of the whole cornea which afterward grew insensitive. After one week, it had healed to one-fourth, the whole cornea remaining insensitive.

4. In the first day the ointment was applied 20 times in seven hours and 39 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of the whole cornea which afterward grew insensitive. After one week, it had healed to one-third, but the whole cornea remained insensitive.

B. *0.5-percent Neotutocain ointment.* Contrary to the effect of the solution, the 0.5-percent ointment had an effect even more prolonged than the two-percent ointment, both in the anesthesia time of each application and in the over-all anesthesia. The results with the four rabbits of the series were:

1. In the first day the ointment was applied 14 times; on the second day, 13 times in eight hours; and on the third day, four times in one hour and 10 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of four-fifths and the whole cornea afterward became insensitive. In one week the erosion healed completely and the insensitive area disappeared.

2. During the eight hours of the first day the ointment was applied 11 times; in the eight hours of the second day, nine times; and in the third day twice in 20 minutes. The rabbit then showed an erosion of three-fourths of the cornea which later became entirely insensitive. In one week the erosion healed completely and the insensitivity disappeared.

3. In the eight hours of the first day the ointment was applied 13 times; in the second day three times in 59 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of one-fourth of the cornea which afterward became insensitive in the area of the erosion. In one week the erosion healed to one-tenth which remained insensitive.

4. In the eight hours of the first day I applied the anesthetic ointment 12 times; in the second day three times in one hour and 34 minutes when the anesthetic lost its effect. The rabbit showed an erosion of one-fourth which afterward became insensitive. In one week the erosion healed and the insensitivity disappeared completely.

C. *Using 0.2-percent Nupercaine ointment.* The anesthetic time of each application was somewhat longer than that of the Neotutocaine ointments (either 2.0 or 0.5 percent), but the anesthetic lost its effect earlier so that anesthesia stopped after fewer applications, and lasted less time than with Neotutocaine, giving an over-all result similar to the solution. The results with the four rabbits of the series were:

1. I applied the ointment nine times in six hours and 32 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of one-fifth, afterward the whole cornea became insensitive. In one week the erosion and the insensitive area disappeared completely.

2. The ointment was applied 10 times in six hours and 39 minutes, the anesthetic then losing its effect. The rabbit showed an erosion of one-third the whole cornea which later became insensitive. In one week the erosion and the insensitive area disappeared completely.

3. The ointment was applied nine times in five hours and 51 minutes, the anesthetic then losing its effect. The rabbit then showed an erosion of one-eighth. Afterward an area of one-half, which comprized the erosion, became insensitive. In one week the erosion and the insensitive area disappeared completely.

4. The anesthetic ointment was applied 12 times in six hours and 39 minutes, the anesthetic then losing its effect. The rabbit showed an erosion of one-third the cornea. Afterward the whole cornea became insensitive. In one week the erosion healed and the insensitive area disappeared completely.

D. *Using a 10-percent cocaine ointment.* The anesthetic effect of each application lasted as long or even longer than one with Nupercaine, but the anesthetic lost its effect

after more applications so that the over-all time of anesthesia was much longer. The results with the four rabbits of the series were:

1. In the eight hours of the first day the ointment was applied nine times; during the second day, eight times in five hours and 43 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of one-third. Later the whole cornea became insensitive. In one week the erosion healed to one-fourth and the insensitive area was reduced to one-fourth, coinciding with the erosion.

2. During the eight hours of the first day the ointment was applied five times, eight hours of the second day, seven times; eight hours of the third day, eight times; and on the fourth day, five times in four hours and 56 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of two-thirds of the cornea which later became insensitive. In one week the erosion healed to one-tenth and the insensitive area disappeared.

3. During the eight hours of the first day the ointment was applied 10 times; eight hours of the second day, eight times; eight hours of the third day, seven times; eight hours of the fourth day, seven times; on the fifth day twice in 45 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of three-fourths of the cornea which later became insensitive. In one week the erosion was as extensive but the cornea grew turbid under it. The insensitive area enlarged to cover the whole cornea.

4. During the eight hours of the first day the ointment was applied nine times; eight hours of the second day, six times; eight hours of the third day, five times; eight hours of the fourth day, six times; and on the fifth day, twice in 45 minutes when the anesthetic lost its effect. The rabbit then showed an erosion of three-fourths of the cornea which later became insensitive. In one week the erosion healed to one-tenth, the same area staying insensitive.

There still remained the possibility that the erosions were caused by the mechanical action of the wisp of cotton, even though that seemed to be implausible as the erosions bore no relation to the number of applications but rather to the quality of the anesthetic. In order to clear up that possibility an experiment was made with two rabbits:

One rabbit had both eyes anesthetized by applying ointment whenever the anesthesia stopped in one of the eyes, the control eye. The other rabbit had the ointment applied whenever the anesthesia stopped in the control eye of the first rabbit. So three corneas were anesthetized with just one of them being touched by the wisp of cotton.

The anesthetic used, a 0.2-percent Nupercaine ointment, lost its effect on the control eye after being applied eight times over a period of six hours and 35 minutes. The control eye then had an erosion of two-thirds the cornea and an insensitive area of four-fifths which included the erosion. The cornea of the other eye of the first rabbit (the one with the control eye) had an erosion of nine-tenths and total insensitivity. The cornea of the anesthetized eye of the other rabbit had an erosion of one-half and total insensitivity.

Discussion

It was shown that topical anesthesia of the cornea by anesthetic ointments has similar secondary effects as anesthesia with anesthetic solutions. There was the same formation of erosions and insensitive areas after more or less prolonged application and the anesthetic effect was always lost. The differences were that the vanishing of the anesthetic effect was not a gradual one, as with the solution, and that the time which the different anesthetics held their effect was not always the same as with the corresponding solution of the same concentration.

With the solution there is a marked diminishing of the over-all anesthesia time from the two-percent solution which held the anesthesia for more than eight hours to the 0.5-percent one that held it for less than eight hours. With the ointments the opposite happened—the two-percent one gave a shorter anesthesia than the 0.5-percent one (table 1).

Nupercaine (0.2 percent) gave more or less the same results applied as a solution or as an ointment. Most striking is the prolonged effect of 10-percent cocaine ointment opposed to the short effect of the solution (less than seven hours).

The erosions and insensitive areas caused were equal or greater with ointment than with the corresponding solution. I think that these effects may be easily explained by the more prolonged contact between the cornea and the anesthetic with the ointment. There remains little doubt that anesthetics cause these secondary effects for they occur with the ointment, too, and the erosions occur even if the cornea is not abraded, as shown by the last experiment.

TABLE 1

FINDINGS IN STUDY OF SECONDARY EFFECTS OF TOPICAL ANESTHESIA OF THE CORNEA

Anesthetic Used	Rabbit	Length of Anesthesia (hr)	No. of Drops Instilled +†	Erosion after Losing Effect	Insensitivity after Losing Effect	Erosion after One Week	Insensitivity after One Week
Neotutocaine (2.0 percent)	1	8+1.24*	16+4	1	1	1.10	2/3
	2	8+2.21	16+7	1	1	1/9	1/3
	3	8+2.50	12+4	1	1	1/4	1
	4	7.39	20	1	1	1/3	1
Neotutocaine (0.5 percent)	1	8+8+1.10	14+13+4	4/5	1	0	0
	2	8+8+0.20	11+ 9+2	3/4	1	0	0
	3	8+0.59	13+ 3	1/4	1/4	1/10	1/10
	4	8+1.34	12+ 3	1/4	1/4	0	0
Cocaine (10 percent)	1	8+5.43	9+8	1/3	1	1/4	1/4
	2	8+8+8+4.56	5+7+8+5	2/3	2/3	1/10	0
	3	8+8+8+8+0.45	10+8+7+7+2	3/4	3/4	3/4	1
	4	8+8+8+8+0.45	9+6+5+6+2	3/4	3/4	1/10	1/10
Nupercaine (0.2 percent)	1	6.32	9	1/5	1	0	0
	2	6.39	10	1/3	1	0	0
	3	5.51	9	1/8	1/2	0	0
	4	6.39	12	1/3	1	0	0

* 8 + 1.24 = 8 hr., 1st day; 1 hr., 24 min., 2nd day.
† To time anesthetic lost its effect.

SUMMARY

It has been demonstrated that continued topical anesthesia by common anesthetic ointments causes the anesthetic to lose its effect and produces erosions and insensitive areas, as occur with solutions of the same anesthetics.

Caixa Postal 878.

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OCULAR MANIFESTATIONS OF THE FULLER-ALBRIGHT SYNDROME*

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In 1937 Albright[1] and his associates described a syndrome characterized by:

1. A disseminated osteitis fibrosa (both hyper- and hypo-ostatic) wtih a distribution suggesting a relationship between the lesions and nerve roots or an embryologic defect in the myotome.

2. Areas of cutaneous pigmentation which have a distribution suggesting some connection between them and the bone lesion.

3. Sexual and somatic precocity, especially if not exclusively, when the disease occurs in the female sex.

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ETIOLOGY

Albright[1,2] felt that the distribution of the bone and cutaneous lesions was such as to preclude an endocrine or metabolic disorder as the cause. In view of the fact that

in one of the cases reported by Albright[1,2] the abdominal and cremasteric reflexes were absent on the same side as the bone lesions and pigmentation, disseminated neurologic lesions were considered as a possible cause. An embryologic defect also seemed possible. The possibility that the gonadal disturbance in this condition might be due to a disturbance in the afferent impulses to the anterior pituitary was also discussed by Albright.[1,2] There is evidence in the literature that sexual precocity may be due to lesions of the walls of the third ventricle and of the hypothalamus.[1]

Lichtenstein,[3] according to Snapper,[4] who refers to this condition as multiple fibrous dysplasia (whereas Albright called it osteitis fibrosia disseminata), suggests that this disease may be due to an anomalous function of the bone-forming mesenchyma. Under normal conditions, this tissue forms spongy bone and normal marrow tissue; however, in polycystic fibrous dysplasia, the bone-forming mesenchyma would give rise to a proliferating fibrous tissue in which scanty fibrous bone particles are still found.

Pathology

According to Snapper,[4] Lichtenstein's[3] summary of the bone lesions in this condition are: (1) Broadening or expansion of the bone, (2) thinning of the cortex, and (3) rarefied and apparently trabeculated appearance of the bone, giving the impression of cyst formation.

The peculiar cystlike appearance of the bone lesions is not due to the formation of actual cavities but because the spongy bone is replaced by a gritty, grayish, fibrous tissue in which specules of insufficiently calcified bone and sporadic islands of hyaline cartilage are formed.

Signs and Symptoms

As already stated this condition is characterized by a disseminated osteitis fibrosa affecting the long bones, pelvis, and skull, pigmentation of the skin, and sexual precocity, especially in the female.

The serum calcium and phosphorus are within normal limits. The serum phosphatase may be elevated.

Ocular signs and symptoms

A survey of the literature reveals, that orbital involvement in this condition, with displacement of the globe, has been reported by Webb[5] and by Albright.[1,2]

Webb's[5] case was that of a five-year-old girl who complained of pain in the left hip, with difficulty in walking. There was a depression of the globe (fig. 1) and radiographic changes in the skull (fig. 2). X-ray studies of the long bone and pelvis showed characteristic changes. A biopsy of the left frontal bone showed changes characteristic of polycystic fibrous dysplasia.

Of the seven cases reported by Albright,[1,2] Case 1 showed changes in the bones of the right orbit with no displacement of the globe. In Case 3, there was X-ray evidence of involvement of the bones of both orbits and, although no mention is made, the photograph accompanying his description of this case suggests a depression of the right globe.

Fig. 1 (Alfano). Showing depression of left globe in a case of Fuller-Albright syndrome reported by Webb. (Webb, J. R. O.: Proc. Roy. Soc. Med., **42**:558, 1949.)

Fig. 2 (Alfano). Same case, showing radiographic changes in left skull and orbit. (Webb, J. R. O.: Proc. Roy. Soc. Med., **42**:558, 1949.)

Fig. 3 (Alfano). Pigmentation of the skin of the right forehead and eyelid in a case reported by Albright.[1] (A) Indicates involvement of the opposite bony orbit as indicated by X rays. (Albright, F., et al.: New England J. Med., **216**:727, 1937.)

Case 4 showed bony involvement of both orbits with pigmentation over the right forehead and upper lid (fig. 3). Case 5 showed bony involvement of the right orbit but no mention is made of displacement of the globe. Case 7 showed a marked prominence of the right side of the head, with exophthalmos (fig. 4) of the right eye and a dilated pupil. Both pupils reacted well to light and accommodation.

Albright[6] calls attention to the fact that of the 25 cases of this condition which have come to his attention, hyperthyroidism was present in two instances. However, in neither of these two cases, the first reported by Albright,[1] and the second by McCane,[6] was any mention made of ocular signs of thyrotoxic exophthalmos.

According to Albright,[1] in the skull the bones most commonly involved are those in the base and the inferior portions of the orbital and frontal bones.

It would appear from this survey of the cases reported, that changes in the bones of the orbit are commonly present and displacement of the globe would depend upon the stage at which the patient is seen.

In contradistinction to polyostotic, polycystic, fibrous dysplasia, there is a condition of monostatic fibrous dysplasia which appears to be unrelated to the former condition and which may produce similar changes in the bony orbit. Two such cases were reported by King and Hayes[7] (fig. 5-A and B). In these two cases there were no areas of pigmented skin or abnormal distribution of hair. A skeletal survey showed no other lesions of the bones. Blood calcium and phosphorus levels were normal. King and Hayes also mention that, while the possibility of future development of additional bone lesions could not be denied, no evidence of the polyostatic form could be found during the patients' hospital stay. The possibility of monostotic fibrous dysplasia being due to localized trauma was considered.

Case Report

History. This is the case of an eight-year-old white boy, who was admitted to the hospital because of pain in the right hip of six months' duration which had resulted in a slight limp. Shortly before admission the child had sustained a fracture of the right humerus after being struck with a fist

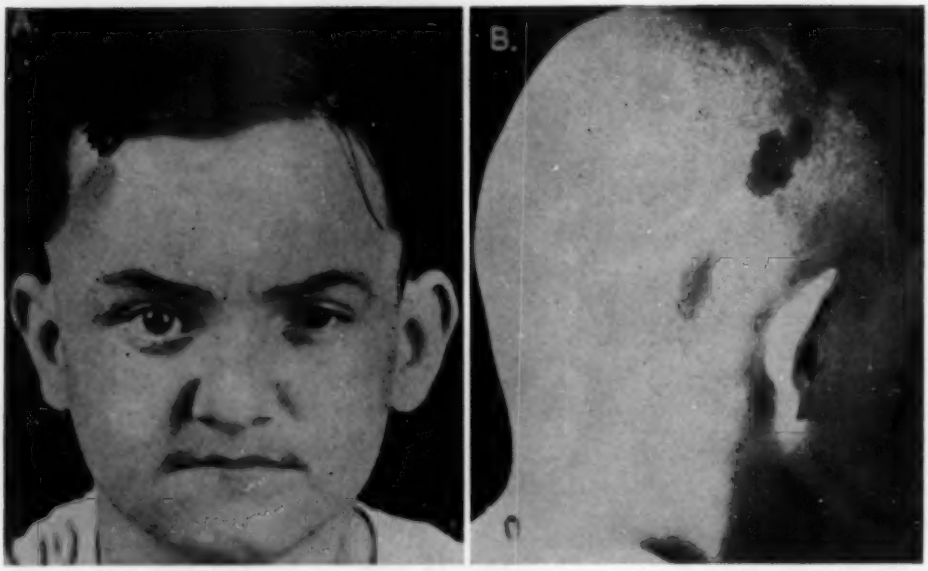

Fig. 4 (Alfano). (A) Demonstrates marked prominence of the right side of the head with exophthalmos and a somewhat larger pupil of the right eye in a case reported by Albright.[2] (B) Showing the pigmentation of the skin of the scalp in the same case. (Albright, F.: Endocrinology, **22**:411, 1938.)

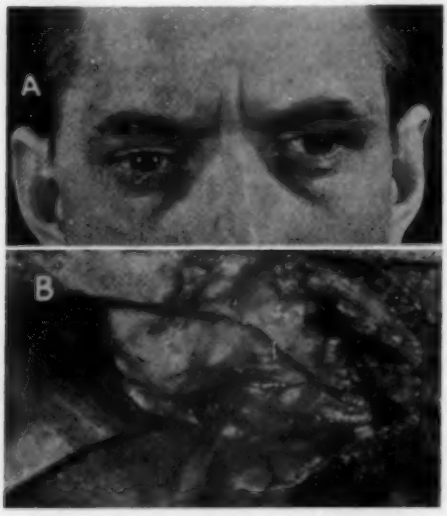

Fig. 5 (Alfano). (A) Showing a depression of the right globe in a case of monostatic fibrous dysplasia, affecting the roof of the orbit only, in case reported by King and Hayes.[1] (B) Same case, showing marked bony prominence of roof of the orbit as seen at surgical exploration. (King and Hayes: Arch. Ophth., **46**:58, 1951.)

by another child. The fracture had healed uneventfully after two weeks. The child had had spots on his body since birth.

Birth and development were considered normal, and the family history was noncontributory.

The child's mother stated that, during the past two years, she had noticed that the left eye was gradually being pushed slightly downward. During this time, the child had complained of intermittent "double-vision."

The physical examination revealed a pleasant, fairly well-developed white boy in no distress, who appeared somewhat small for his age (figs. 6A, 6B, and 6C). Physical examination was completely normal excepting that:

1. The frontal area of the head was flattened and appeared somewhat square in shape. The fontanelles were closed.

2. The extremities were normal except for slight swelling of the upper portion of the right arm.

3. There were scattered, dark-brown pigmented lesions over the upper chest and a ribbonlike pigmented area extending from the neck downward over the upper cervical region.

The eye findings (figs. 7 and 8) were:

The patient complained of no loss of vision. There was some diplopia on upward gaze. Although visual acuity was not checked with the usual charts, the patient could see very well to read his books and play with the other children in the ward.

External examination revealed the left eye to be

Fig. 6 (Alfano) (A) Photograph of patient, showing slightly underdeveloped, white boy (front view). (B) Lateral view. (C) Posterior view, showing pigmentation of the skin of the back of the neck in the midline.

displaced vertically downward. While indefinite, palpation revealed some thickening of the superior lateral wall of the orbit. Pupillary reactions were normal. Horizontal ocular rotations were normal. Vertical rotations revealed a definite limitation of

Fig. 7 (Alfano). Anterior view of face of patient, showing a depression of the left globe, with prominence of the superior and lateral orbital bony margins. There is a suggestion of fullness of the left upper lid.

Fig. 8 (Alfano). Lateral view of patient, showing prominence of left forehead and outer aspect of orbital margin.

upward motion of the left eye. Both fundi were normal, as were confrontation visual fields and corneal sensation.

Roentgenologic examination of the skeleton revealed (fig. 9 to 15):

1. Posterior-anterior occipital and lateral views of the skull revealed a marked sclerosis around the left orbit (figs. 9 and 10). Stereoscopic examination of the left optic foramen (fig. 11) compared with a single view of the right optic foramen suggested that this sclerosing process extended back into the left orbit and optic foramen as well.

2. A lateral (fig. 10) view of the skull showed a suggestive thickening of the base of the skull and the floor of the frontal fossa.

3. There were irregular radiolucent areas throughout the shaft of both humeri (fig. 12) and a well-healed fracture of the right humerus. Radius and ulna were normal (fig. 13).

4. There were irregular radiolucent areas in the right upper femur and the neck of the right and left femurs (fig. 14). There was a suggestion of a fracture through the middle cortex of the left femur. These same radiolucent areas were seen in the tibia and fibula as well (fig. 15). Irregular areas of bone destruction were present in the right and left ilium (fig. 16).

5. Intravenous pyelograms were normal. There was no bone involvement of the spine.

The impression of the radiologist was that these

Fig. 9 (Alfano). Posterior-anterior view of skull, demonstrating marked sclerosis around the left orbit.

Fig. 11 (Alfano). Stereoscopic examination of the left optic foramen suggested that the sclerosis also extended back into the region of the left orbit and optic foramen.

Fig. 10 (Alfano). Lateral view of skull showing a marked sclerosis around the left orbit and a suggestive thickening of the base of the skull and the floor of the frontal fossa.

Fig. 12 (Alfano). X-ray views of both humeri, demonstrating irregular radiolucent areas throughout both shafts.

Fig. 13 (Alfano). X-ray film, demonstrating normal radii and ulna.

multiple, asymmetric fibrous areas in the skeleton, associated with the sclerosis of the bones of the left orbit, were presumably due to polycystic fibrous dysplasia occurring in a male.

All the laboratory studies were consistent with the diagnosis of polycystic fibrous dysplasia. Blood

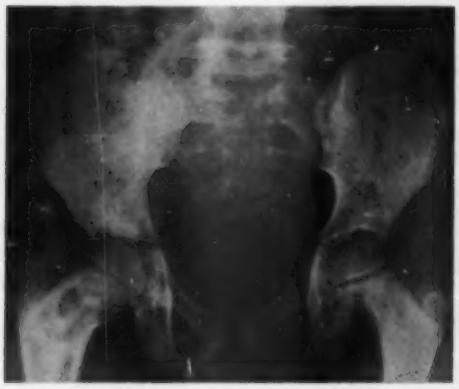

Fig. 14 (Alfano). X-ray film, demonstrating multiple irregular radiolucent areas in the right upper femur and the neck of the right and left femurs. Irregular areas of bone destruction were present in the right and left ileum.

Fig. 15 (Alfano). X-ray view of tibia and fibula, demonstrating irregular radiolucent areas.

chemistries were all normal except for an elevated alkaline phosphatase.

The Mantoux skin test was negative, as was the serologic test for lues. Urine was normal.

Red blood cell count, white blood cell count, and differentiated counts were considered normal, as was the hemoglobin determination. Blood platelet determination was normal (150,000), and the bleeding time was five minutes (normal 1-3 minutes).

The remaining blood chemistries are shown in Table 1.

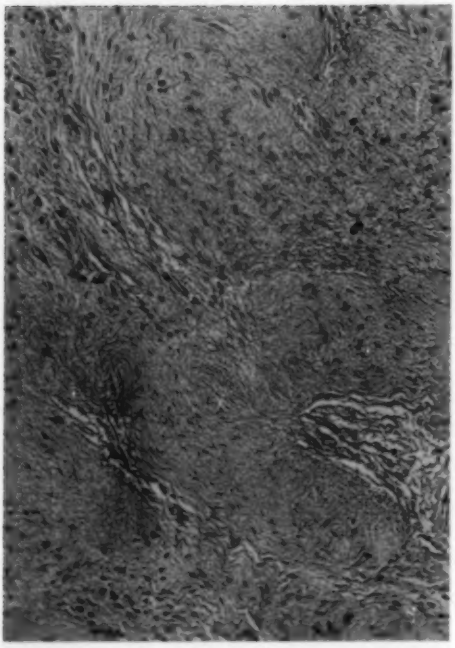

Fig. 16 (Alfano). Microscopic section of bone fragments removed for biopsy, showing replacement of marrow space by moderately cellular and somewhat edematous and myxomatous-appearing fibrous tissue (×120).

On one occasion, the urine Sulkovitz reaction for calcium was negative, while a second determination was one plus.

On one occasion, the urine 17 ketosteroid determination performed on a 24-hour specimen of 640 cc. revealed 2.56 mg. per total volume; a second determination performed on a total volume of 210 cc. was found to be 1.24 mg. per total volume.

A biopsy of the right femur was performed, and two portions of tissue were received for pathologic examination. The first consisted of a quantity of tiny osseous fragments aggregating to a mass of one gram. The second portion of tissue consisted of skin and subcutaneous tissue; the strip of skin measured 2.5 cm. in length and 0.4 cm. in width. The subcutaneous tissue measured 1.5 cm. in depth. There was nothing remarkable on gross examination.

Sections of the osseous (fig. 16) fragments revealed them to be composed of anastomosing long trabeculas of normal histologic contour. The marrow spaces were completely replaced by a moderately cellular and somewhat edematous myxomatous-appearing fibrous tissue. The nuclei were predominantly spindle-shaped and stellate in outline. There were occasional lymphocytic cells distributed throughout the myxomatous stroma. Other sections revealed the tissue to be composed almost entirely of a dense, interlacing fibrous stroma, with closely-packed, plump, ovoid nuclei. Embedded within this tissue were minute, irregular islands of mature-appearing bone, around which at various sites clusters of osteoclasts could be identified. These islets of osseous tissue appeared different from the normal bony specules that are usually found in the marrow cavities. That this bone was being produced by the tissue seemed most probable, and may in part account for the elevated alkaline phosphatase noted clinically.

Sections through the skin and subcutaneous tissue revealed the epidermal lining to be intact and of normal appearance. Elastic tissue fibers were brought out by special staining and a normal aggregate of elastic tissue was found within the dermis.

A chromosomal sex determination was made by counting 100 cells in the Malpighian layer of the epidermis and identifying the number of cells containing XX chromosomes. The percentage of such

TABLE 1

BLOOD CHEMISTRY STUDIES

	Patient's Values	Normal Range
Blood glucose	74 mg.%	80–120 mg.%
Nonprotein nitrogen	37 mg.%	35 mg.%
Urea nitrogen	14 mg.%	15 mg.%
Total protein	7.7 mg.%	
Albumin	5 mg.%	3.7–4.7 mg.%
Globulin	2.7 mg.%	1.3–2.3 mg.%
Sodium	147.98	138–146 m.eq/L.
Potassium	5.08	4.1–5.4 m.Eq/L.
Calcium	10.4	10– 12 mg.%
CO_2 combining power	26.5	25– 29 m.Eq/L.
Chlorides	105.0	99–108 m.Eq/L.
pH	7.60	7.35–7.50
Phosphatase	20.6	5–12 units
Cholesterol	204	114–209 mg.%

A cephalin-flocculation test for hepatic dysfunction was 3+.

cells aggregated to 30, indicating that the individual is presumably male.

The impression was that the histologic picture was compatible with fibrous dysplasia, showing some osteoblastic activity.

Differential diagnosis

This condition must be differentiated from those general or systemic disorders which may produce somewhat similar changes in the skeleton and skull, including, primarily, von Recklinghausen's disease, and Hand-Schüller-Christian disease. Less often a similar picture may result in Paget's disease, and hyperthyroidism.

This condition must necessarily also be differentiated from those conditions, more or less localized to the orbit, which may give rise to sclerosis and hyperostosis of the orbital margin and bones. These conditions include: (1) Meningiomas arising from the sheaths of the optic nerve either within or out of the orbit; meningiomas arising in the arachnoid in the olfactory groove or along the sphenoidal ridge, spreading along the cranial vault and finally penetrating the bone to enter the orbit. Less common causes are hemangiomas or neurofibroma of the cranial vault or orbit and chronic orbital inflammation. Localized hyperostosis (fig. 16) may also occur in leontiasis ossea, yaws, and acromegaly. A simple hyperplasia or calus formation may occur after traumatic fractures involving the outer orbital wall.

Von Recklinghausen's disease. The changes in this condition are now known to be the result of a hyperparathyroidism resulting from an adenoma of the parathyroid glands. This condition is characterized by severe aching of the bones, generalized osteitis fibrosa, spontaneous fractures, brown spots or tumors in the skin, hypercalcemia, hypophosphatemia, increased calcium and phosphorus content of the urine, renal calculi, unexplained fatigue and polyuria, occasional muscular hypotonia, and vomiting.

The X-ray pictures of the skeleton are characteristic of renal fibrous osteitis, the skeleton giving the appearance of old decayed wood full of pores. The presence of one or more honeycomblike giant-cell tumors in the bones of the skull is a strong point in favor of a diagnosis of von Recklinghausen's disease.

Since the condition is a combination of an absorptive and formative process so that the bone is replaced by fibro-osteoid tissue, hyperostosis of the skull may result when healing sets in. When this process affects the bones of the roof of the orbit (frontal), displacement of the globe and optic atrophy may result.

Hand-Schüller-Christian disease is lipoid granulomatosis of a special kind of granulomatous tissue in the skeleton. The sites of predilection are the skull and pituitary region which give rise to round areas of decalcification in the skull, exophthalmos, diabetes insipidus, and infantilism. In many cases areas of cystic lipoid granuloma are found in the long bones, pelvis, and spine. Occasionally this condition may affect the long bones only without craniopharyngeal involvement, causing confusion with the Fuller-Albright syndrome and von Recklinghausen's disease. In Hand-Schüller-Christian disease, xanthomatous plaques may affect the orbital cavity, producing a displacement of the globe.

Eosinophilic granuloma, which may prove to be a monostatic form of Hand-Schüller-Christian disease, is characterized by the rapid appearance of a swelling in a bone, usually the skull, and may affect the roof of the orbit with subsequent displacement of the globe. The typical biochemical changes of hyperparathyroidism are not seen in the Hand-Schüller-Christian disorders.

Paget's disease. This condition is characterized by the absorption and new formation of bone, leading to enlargement of the skull, bowing of the limbs and clavicle, and on sometimes to nervous symptoms secondary to bone changes. Paget's disease hardly ever occurs in persons under the age of 40 years and, even in the most extensive cases,

many parts of the skeleton remain free from the affection.

Ocular complications are not uncommon and are the result of a diminished orbital capacity produced by the formation of new bone.

In Paget's disease, the serum calcium and phosphorus values are normal, as are the values for the excretion of calcium and phosphorus in the urine. There is, however, an increase in the serum phosphotase.

Hyperthyroidism. In many cases of Graves' disease, a certain degree of decalcification of the skeleton may occur and, in some cases, may be present to such a degree as to be confusing. Only rarely in Graves' disease does the decalcification of the skeleton produce a fibrous osteitis.

To distinguish those localized conditions which may cause confusion, Duke-Elder[8] defines a hyperostosis as a diffuse thickening of the bone due to an irritative condition in the adjacent soft tissue, or an invasion of its substance by neoplastic cells. The lesion is diffuse without defined margins and the growth consists of superimposed layers of eburnated bone or of cancellous tissues which sometimes have cystic spaces. Such thickenings are found in the roof of the orbit, the apex, over the large wing of the sphenoid, and particularly along the sphenoidal ridge.

Meningioma[8] of the optic nerve sheaths, olfactory grooves or sphenoidal ridge may produce hyperostoses of the adjacent orbital roof and wall. Optic nerve sheath meningiomas usually give rise to visual loss, exophthalmos with frequent depression of the globe, restricted ocular motility, either edema or atrophy of the nervehead, and roentgenologic changes affecting the involved orbit and optic foramen. Olfactory groove meningiomas may give rise to an anosmia, optic atrophy with visual loss, defects in the visual fields, and, in some cases, personality defects due to involvement of the frontal lobes. Occasionally the Foster-Kennedy syndrome is seen.

Sphenoidal ridge meningiomas[8] may produce unilateral exophthalmos, with unilateral visual loss, optic atrophy, and defects in the visual fields. Changes in the sphenoidal ridge are usually seen on X-ray examination.

Suprasellar meningiomas give rise to a visual loss associated with a bitemporal type of defect in the visual fields. Later there may be X-ray evidence of destruction of the sella, and endocrine disturbances may develop.

Hemangioma[8] in or in the region of the orbit will usually give rise to a slowly progressive, painless proptosis which tends to be compressible, may be pulsile, but never exhibits a bruit. Ocular motility may be surprisingly good.

Neurofibromas of the optic-nerve sheath exhibit no clinically distinguishing features from other nerve-sheath tumors, except for

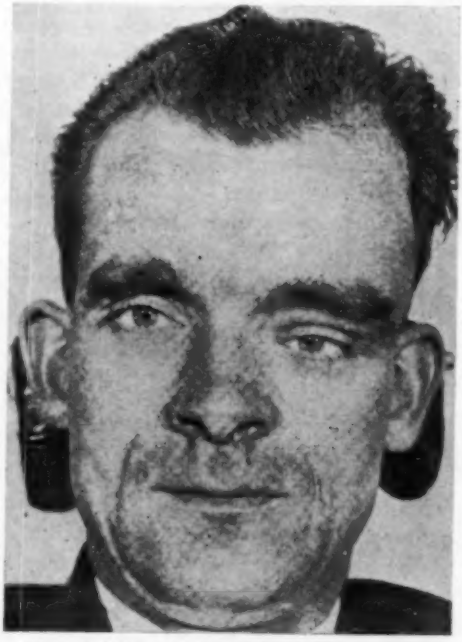

Fig. 17 (Alfano). Prominence of the left forehead and orbital margin, with depression of the left globe in a case of localized, monostatic leontiasis ossea. (Phelps: [fig. 4.] Brit. J. Ophth., **23**:734, 1939.)

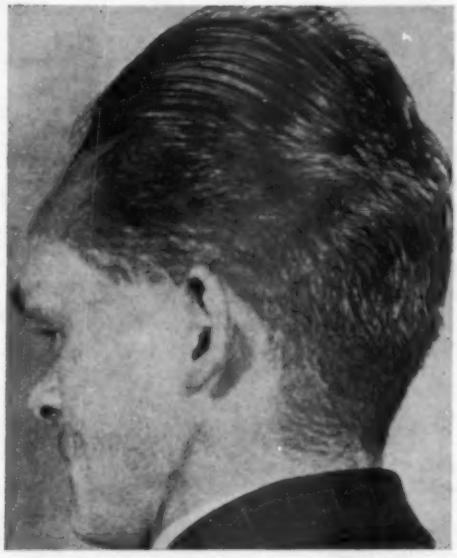

Fig. 18 (Alfano). Lateral view of the same case showing marked prominence of left forehead. (Phelps, S.: [fig. 5] Brit. J. Ophth., **23**:734, 1939.)

the frequent association of the manifestations of von Recklinghausen's disease such as café-au-lait spots.

According to Phelps[9] leontiosis ossea may manifest itself as a generalized or localized thickening of the bones of the skull and face. If the disease is localized to the orbital bones only, it gives rise to an enlargement of the frontal region, causing a downward displacement of the globe (figs. 17 and 18). In both forms of the disease, even though there is a proptosis and the globe is considerably displaced, there may be no visual symptoms. At times optic atrophy may occur.

Acromegaly usually affects the orbit as a thickening of the orbital margins. Other signs of acromegaly, resulting from an eosinophilic adenoma of the pituitary, are usually in evidence. These include osseous overgrowths in the skull, face, mandible, feet, and dorsal spine. Defects may or may not be present in the visual fields, with or without changes in the sella turcica.

Conclusion

A case of Fuller-Albright's disease is reported. The syndrome consists of polycystic fibrous dysplasia, pigmentation of the skin, and sexual precocity in the female. Serum calcium and phosphorus are normal, although the alkaline phosphatase value may be elevated. Involvement of the bones of one or both orbits may be present, producing a downward displacement of the globe and diplopia. The differential diagnosis is discussed.

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IMMUNIZATION AGAINST HERPES KERATITIS IN RABBITS*

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Herpes simplex is one of the most frequent virus infections in man. The primary infection usually takes place in early childhood, mostly in the form of a subclinical infection. Only few of the primary infections manifest themselves as a disease: gingivostomatitis, vulvovaginitis, varicelliform eruption, and so forth. After the primary infection, the virus often persists in a latent form during the rest of the patient's life and may cause recurrent manifestations. Herpes simplex tends to recur in the same skin area, following nonspecific stimuli which may be either of a general or a local nature. "Inoculation herpes" in traumatic skin lesions may also lead to recurrent herpes at the site of the original injury. In general, herpes simplex shows a predilection for areas of mucocutaneous junctions.

The cornea is one of the sites of predilection of herpes simplex. Most cases of herpes keratitis are of the recurrent type. Occasionally, however, cases of primary corneal infection have been recognized by means of serologic methods (Gallardo, 1943).

Various investigators have studied the possibility of immunization against herpes keratitis. The results of these studies are contradictory in part and do not lead to preventive measures. Recurrent herpes blisters and herpes keratitis occur in persons with a high blood level of virus-neutralizing antibodies. This suggests that either latent virus need not contact humoral antibodies on its way to susceptible host cells, or such contact would be ineffective from an immunologic point of view.

Table 1 shows the high virus-neutralizing potency of sera originating from patients with recurrent herpes. The neutralization index was determined with a virus dilution method (Gispen, 1953). The presence of herpes antibodies in human sera is shown by the high neutralization index of pooled sera of 100 Wassermann-negative persons, and of a sample of human gamma globulin supplied by the Central Laboratory of the Blood Transfusion Service, Amsterdam. In all these cases, the neutralization index ranges from 10^3 to 10^4. This high potency in vitro is not in agreement with the hypothesis that these antibodies might be inactive in vivo. It should rather be assumed that the localization of the latent virus is such that when a recurrence is elicited, previous transport of the virus through the blood stream is unnecessary. During the interval between two recurrences, the virus may be hidden in the host cells of the site of predilection.

If, however, during an ocular manifestation the virus in corneal lesions would be more exposed to locally applied antibodies, the effect of local serum treatment upon herpes keratitis should be examined. We made some preliminary experiments of this kind in rabbits, granting a request of Prof. A. Hagedoorn, Amsterdam. As therapeutic use of sera has been unsuccessful in virus diseases, it seemed advisable also to consider

TABLE 1

VIRUS NEUTRALIZING ANTIBODIES IN SERA AND BLOOD DERIVATIVES OF VARIOUS ORIGIN

Material	Neutralization Index
Serum, herpes keratitis	10^4
Serum, herpes labialis	10^4
Serum, recurrent herpes	10^3
100 pooled WaR negative sera	10^3
Human gamma globulin (Amsterdam)	10^4
Immune serum rabbit	10^4
Normal human serum (no herpes-simplex history)	10^0–10^1
Normal rabbit serum	10^0

* From the Rijks Instituut voor de Volksgezondheid (National Institute of Public Health).

prophylactic administration of antibodies, though this is impracticable as a preventive measure in man.

The effect of serum treatment was investigated in nine rabbits. The infection was effected under local anesthesia by scarification of the left and right corneas with a dense suspension of infected chorioallantoic tissue originating from duck embryos. Treatment consisted of instillation of immune rabbit serum (neutralization index: 10^4) three times per day into the left eye.

Table 2 shows that the treatment with herpes serum has no effect on the course of the herpes keratitis, even when the treatment is instituted one day prior to the infection.

Four rabbits were subcutaneously inoculated with 1.0 ml. of a formalinized herpes virus suspension (chorioallantois 1:10) and at the end of the second and third weeks thereafter with the same quantity of live virus. These rabbits, which after vaccination showed a high titer of neutralizing antibodies in the blood, showed no protection against corneal scarification with herpes virus (table 3). The cornea is apparently insufficiently protected against virus inoculated directly into the corneal layer. Treating the cornea with herpes serum is of no influence in this respect.

If, however, vaccinated rabbits receive their challenge dose of virus along the intravenous route, the humoral antibodies appear to act as an effective barrier against the infection. The same holds true for the subcutaneaus route of infection. Table 4 represents an experiment in which the vaccinated rabbits are absolutely protected against intravenous injection of a rather high dose of herpes virus, whereas normal rabbits respond for the greater part with a fatal encephalomyelitis.

It is, therefore, not unreasonable to ascribe the failure of active and passive immunization in experimental herpes keratitis

TABLE 2

EXPERIMENTAL HERPES KERATITIS IN RABBITS TREATED WITH RABBIT IMMUNE SERUM (NEUTRALIZATION INDEX 10^4)

Number of Rabbits	Onset of Serum Treatment	Corneal Reaction: Typical Keratitis	
		Left (treated)	Right (untreated)
2	Untreated	+	+
2	1 day after infection	+	+
2	A few hours after infection	+	+
3	1 day before infection	+	+

TABLE 3

CORNEAL INFECTION WITH HERPES-SIMPLEX VIRUS IN VACCINATED RABBITS

Rabbit	Neutralization Index Serum before Infection	Typical Herpes Keratitis after Infection	Result
Vaccinated:			
623	10^3	+	Recovery
627	10^3	+	Recovery
628	10^2	+	Paralysis
629	10^3	+	Recovery
Normal:			
767	10^0	+	Recovery
804	10^0	+	Paralysis
879	10^0	+	Recovery
1	10^0	+	Recovery
2	10^0	+	Recovery

TABLE 4

INTRAVENOUS INFECTION OF VACCINATED RABBITS WITH HERPES-SIMPLEX VIRUS

(Dose: 0.25 ml. one-percent suspension of infected chorioallantois in saline)

Rabbit	Neutralization Index Serum before Infection	Encephalomyelitis (Paralysis) after Infection	Isolation of Virus from Brain and Spinal Cord
Vaccinated:			
1	10^4	−	
7	10^3	−	
2	$>10^3$	−	
9	$>10^3$	−	
Normal:			
67	10^0	+	+
68	10^0	+	+
99	10^0	+	+
100	10^0	−	−

in rabbits to insufficient contact between virus and antibodies. The frequent natural recurrences of herpes in human cornea or skin, notwithstanding a high titer of humoral antibodies, might be explained in a similar way. It is supposed by Burnet (1945) that herpes virus persists in the host cells during the latent period.

Unfortunately all attempts to isolate the latent virus from the tissue of the site of predilection between recurrences have failed so far (Findlay and MacCallum, 1940; Blank, 1948). Nevertheless, the virus could be present in a noninfectious form which might undergo reactivation consequent to certain stimuli. Moreover, incomplete or inactive forms have been demonstrated experimentally as a stage in the multiplication of various viruses.

The epidemiologic, clinical, and immunologic phenomena are also consistent with Burnet's hypothesis. At any rate, the fact that it is very difficult, if not impossible, to protect rabbits by vaccination against intracorneal infection is in agreement with the absence of immunity against recurrent eruption of herpes in the skin and cornea of man.

Summary

A few experiments with active and passive immunization against herpes keratitis in rabbits are described. Herpes keratitis was prevented neither by local treatment of the eye with herpes immune serum nor by vaccination with both formalinized and live herpes virus. However, vaccinated rabbits are immune to herpes encephalomyelitis, if the infective dose is administrated along the intravenous route. It is presumed that the virus in corneal infection does not come into such contact with humoral antibodies that complete neutralization can be effected. Recurrent herpes eruptions in patients with a high titer of humoral antibodies might be explained in a similar way.

Sterrenbos 1.

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CORTICOSTEROIDS IN THE AQUEOUS HUMOR OF THE RABBIT EYE*

Further studies with paper chromatography

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Evidence for the presence of hydrocortisone in normal aqueous humor of rabbit eyes in a concentration of about 3.0 μg./17 ml. was presented in an earlier publication. The subject of this report is concerned with an analysis of the aqueous humor after the removal of the hydrocortisone. The results show that in addition to hydrocortisone rabbit aqueous humor contains a relatively highly nonpolar substance that responds to the NaOH-blue tetrazolium spray test but does not show the fluorescent or chemical properties characteristic of the presence of a Δ^4-3-keto group, at least in concentrations of 1.0 μg. or more per 17 ml.

Materials

Unless otherwise noted all chemicals and solvents were of reagent grade. Formamide was a practical grade obtained from Distillation Products Industries. Toluene, propyleneglycol, benzene, cyclohexane were also purchased from Distillation Products, while absolute methanol and petroleum ether were Mallinckrodt products. Ethyl acetate was obtained from Merck and Company. Toluene, chloroform, and methanol were redistilled prior to use. Blue tetrazolium was purchased from the Nutritional Biochemicals Corporation and used without purification as a 0.2-percent solution and mixed with two volumes of 10-percent NaOH for spraying.

In addition to the cylindrical Pyrex jars, 24-inches high and 12 inches in diameter, previously used, the Research Equipment Corporation Chromatocab was also used. For use in the glass jars Whatman No. 1 filter paper was fashioned into parallel limbs of 1.0 by 30 cm. attached to a common head, while in the Chromatocab 1.0 by 47-cm. strips were used.

A Beckman spectrophotometer model DU was employed to measure the absorption spectra of solutions contained in quartz microcurettes, total volume of 1.0 ml. with a 1.0 cm. light path. A short wave mineralight (Ultraviolet Products Corporation) and a longer wave lamp (320 to 390 mμ, Charles Lentz Company) were used to scan the developed chromatograms.

The following crystalline corticosteroids, kindly supplied by Merck, Sharp, and Dohme, were used as standards for evaluation: hydrocortisone, dihydrocortisone, tetrahydrocortisone, tetrahydro-11-dehydrocorticosterone, 11-dehydrocorticosterone, corticosterone, 11-dehydrocorticosterone acetate, and dihydrocortisone acetate.

Experimental

The overflow of the developing solvent from the initial chromatographic studies was concentrated under reduced pressure to a small volume and applied to paper and dried as previously described. Preliminary inspection of the resulting spot indicated the presence of material that responded to the NaOH-blue tetrazolium spray test.

Because of the possibility that long storage of the overflow developing solvent from the chromatographic separation of hydrocortisone in the aqueous humor may have resulted in the decomposition of corticosteroids present, subsequent studies were conducted with aqueous humor collected over a period of about two to four days. Details of the collection, extraction, and evaporation

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procedures have already been described.[1]

The initial chromatographic separation of hydrocortisone from the chloroform extract of 17-ml. samples of aqueous humor was accomplished by the descending technique of Burton and co-workers[2] using the toluene-propylene glycol system in a Chromatocab, rather than in the glass jar as previously used. In order to avoid the necessity of concentrating the overflow solvent for analysis, the initial chromatograph was run just long enough to prevent the developing solvent from running off the paper.

At the end of from two to four hours, depending upon atmospheric conditions, the solvent front had descended to within five to 10 cm. of the bottom of the 47-cm. strip of Whatman No. 1 paper, while hydrocortisone was identifiable just below the origin. Inspection of the dried chromatogram revealed an area within two cm. of the solvent front to be faintly positive to the NaOH-blue tetrazolium spray test and to show a very faint fluorescence when examined by the ultraviolet scanner. Elution of this excised area with 1.0 ml. of absolute methanol for one hour followed by spotting of the solution, which had been concentrated in vacuo, on to paper gave a spot which was clearly positive to blue tetrazolium but showed no ultraviolet fluorescence.

Rechromatography

Successful chromatographic separation of the material eluted with methanol from the solvent front area of the initial chromatogram required the use of a solvent system in which the mobility of the material was different from that of the developing solvent front. Preliminary trials with some solvent systems established that the cyclohexane-benzene formamide (350:350:80) system of Zaffaroni[3] in descending chromatography possessed suitable resolving power. The other solvent systems tried were: Benzene-ethylacetate-H_2O (200:10:50)[4] and petroleum ether (30-60°)-propylene glycol (300:80).

The chromatographic procedure adopted was as follows:

The methanol eluate of the solvent front area of the chromatogram developed for the separation of hydrocortisone was concentrated in vacuo to a volume of about 0.5 ml. and applied to paper strips as previously described. The paper had been fashioned into 1.0 by 30 cm. strips and impregnated with formamide (50 percent in CH_3OH by vol.), the excess having been removed by blotting with absorbent paper.

Chromatography was performed by the descending technique of Burton and co-workers,[2] using formamide-saturated cyclohexane-benzene (350:350:80) as the developing solvent. For more rapid and efficient resolution slightly elevated temperatures (28 to 30°C.) were used. This was achieved most readily in glass jars, as previously described, in a special warm area of the laboratory. A constant saturated atmosphere was maintained throughout the chromatography by lining the walls of the jars with large sheets of filter paper dipping into developing solvent on the bottom.

When the solvent front had descended to within five to 10 cm. of the bottom of the paper, the paper was removed from the jar and dried in the dark in a gentle stream of warm air for about 12 hours.* The zone corresponding to the blue tetrazolium positive area of a parallel strip was eluted with methanol for about one hour and the resulting solution was examined spectrophotometrically. Evaporation of the methanol extract and treatment of the residue with concentrated H_2SO_4 gave a H_2SO_4-chromogen whose spectrum was also determined.

Results

The zone which was visible when the chromatogram was sprayed with blue tetrazolium-NaOH corresponded roughly to about

* Complete drying is necessary to remove traces of solvent that may interfere with the ultraviolet absorption spectrum.

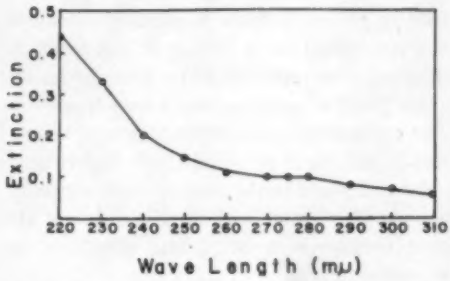

Fig. 1 (Green, Kroman, and Leopold). Ultraviolet absorption spectrum.

1.0 μg. of α-ketol-containing corticosteroid (hydrocortisone used for comparison). The zone was located 13.0 to 15.0 cm. from the origin, while the solvent front had moved 25 cm. in 1.5 to 2.5 hours. Under similar conditions of chromatography all of the known relatively nonpolar corticosteroids examined did not move as rapidly as the indicated zone. No fluorescence on a parallel strip was observed under the short-wave light of the ultraviolet scanner. Similarly, spraying with NaOH-methanol solution did not reveal any yellow fluorescence[5] when examined under the longer-wave light.

Elution with methanol of the blue-tetrazolium positive zone from a parallel strip (untreated with blue tetrazolium) and subsequent spectrum analysis showed no characteristic peak in the range from 220 to 310 mμ, although a slight plateau with an extinction of 0.100 was discernible between 270 and 280 mμ (fig. 1).

The H_2SO_4-chromagen spectrum (fig. 2) showed shallow peaks at 270, 300, and 350 mμ with optical densities of 0.100, 0.077, and 0.042, respectively.

Discussion

The results of this investigation show that in addition to the hydrocortisone previously found to be present in aqueous humor of the normal rabbit eye (3.0 μg./17 ml.) there is a trace of another substance which is chloroform extractable and gives a positive blue tetrazolium test. It is estimated that the intensity of the resulting colored spot corresponded to about 1.0 μg. or less of material.

The chromatographic properties of this substance indicate it to be relatively highly nonpolar compared to the known corticosteroids but not identifiable with any so far tested. The absence of a Δ^4-3-keto group or α, β-unsaturation is suggested by failure of the chromatogram to exhibit fluorescence either when examined with a short-wave ultraviolet scanner or with a longer wave scanner after being sprayed with NaOH-methanol solution. This receives confirmatory support in the fact that the ultraviolet spectrum of the eluted chromatogram showed no characteristic peak at 242 mμ, although the absorption was relatively high in the lower wavelength region.

The limits of detectability of the scanning procedures is about 1.0 μg, while that of the peak at 242 μ is about 0.5 μg. Thus, it can be said that although the presence of an absorption maximum of 270 mμ in the H_2SO_4 chromogen absorption spectrum may be suggestive of the presence of an α, β-unsaturation, lack of confirmation by the

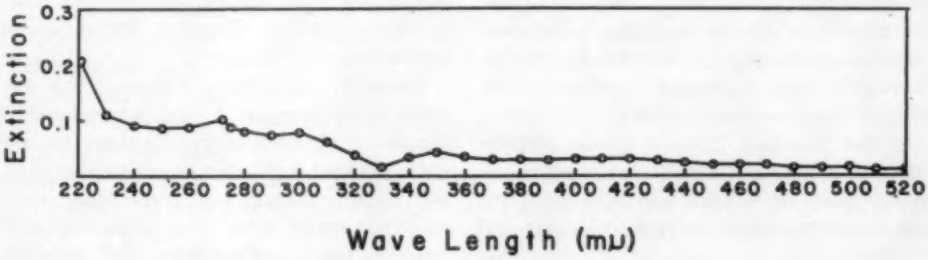

Fig. 2 (Green, Kroman, and Leopold). H_2SO_4-chromagen spectrum.

above more sensitive and direct criteria reduce the probability that this is the case. The substance in question is present in a concentration of 1.0 μg or less per 17 ml. of aqueous humor. More sensitive analytical methods are necessary to characterize it more fully and to determine its actual concentration.

SUMMARY

In addition to the hydrocortisone previously shown to be present in rabbit aqueous humor (3.0 μg./17 ml.), there is another substance in a concentration of 1.0 μg or less which is chloroform extractable and whose chromatogram gives a positive blue-tetrazolium test. The chromatographic properties of this substance indicate it to be relatively highly nonpolar compared to the known corticosteroids, but not identifiable with any. It does not appear to possess a Δ^4, 3-keto group or an α, β-unsaturation.

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BIOCHEMICAL STUDIES ON CATARACT*

IX. CONTRIBUTION TO THE HISTOPATHOLOGY OF CATARACT CAUSED BY VARIOUS QUINOID SUBSTANCES

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In an extensive series of experimental cataracts, we demonstrated various quinoid substances as cataractogenic agents.[1-6] Ogino et al.[1] isolated beta-naphthoquinone combined with cysteine from the urine of rabbits administered naphthalene and determined its cataractogenic activities. Thereafter, the same authors demonstrated that vitamin-C deficient guinea pigs developed cataracts following injection of benzoquinone-acetic acid, one of the abnormal metabolites of tyrosine, and that vitamin-C deficient guinea pigs developed cataracts following simultaneous administration of tyrosine and such ketogenic substances as sodium butyrate, l-leucine, and sodium acetate, identifying benzoquinone-acetic acid excreted in the urine.[2] Ogino et al.[3] established that dopa-quinone and adrenalin-quinone derived from tyrosine also had cataractogenic activities (fig. 1).

Further, it was demonstrated that the production of alloxan-diabetic and galactose cataract is closely related to the abnormal metabolism of tyrosine.[4]

Recently, Ogino et al.[5] showed that the onset of senile cataracts is closely related to the abnormal metabolism of tryptophan, on showing that quinonimine-carboxylic acid, one of the metabolites of tryptophan, could be demonstrated in the urine of patients with senile cataracts and that vitamin-C deficient guinea pigs developed cataracts following in-

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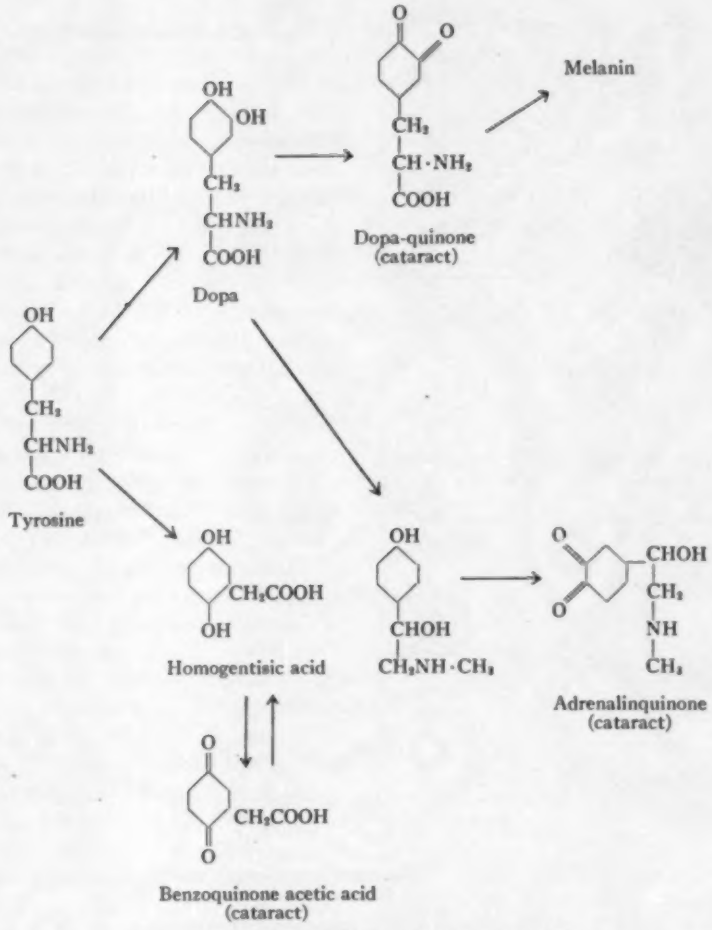

Fig. 1 (Ogino, et al.). Metabolism of tyrosine and cataractogenic substances.

jection of p-quinonimine-carboxylic acid (fig. 2). It was further determined that dinitrophenol cataract was due to 2-amino-p-quinonimine, one of the metabolites of dinitrophenol.[6]

The present study was undertaken to clarify the histologic changes in cataracts caused by the various quinoid substances, such as beta-naphthoquinone, p-quinonimine-carboxylic acid, and 2-amino-p-quinonimine.

Method

1. *Histologic technique.* The histologic technique used in these experiments was as follows:

The eyes of experimental animals were enucleated immediately and fixed in Zenker's and formalin solutions. Specially large sagittal calottes, including the lens, were made in order to facilitate penetration of the celloidin into the lens.

After the eyes were embedded in celloidin, 15 mμ sections were cut at various stages of cataract and were stained with hematoxylin and eosin.

2. *Quinonimine-carboxylic acid cataract.*

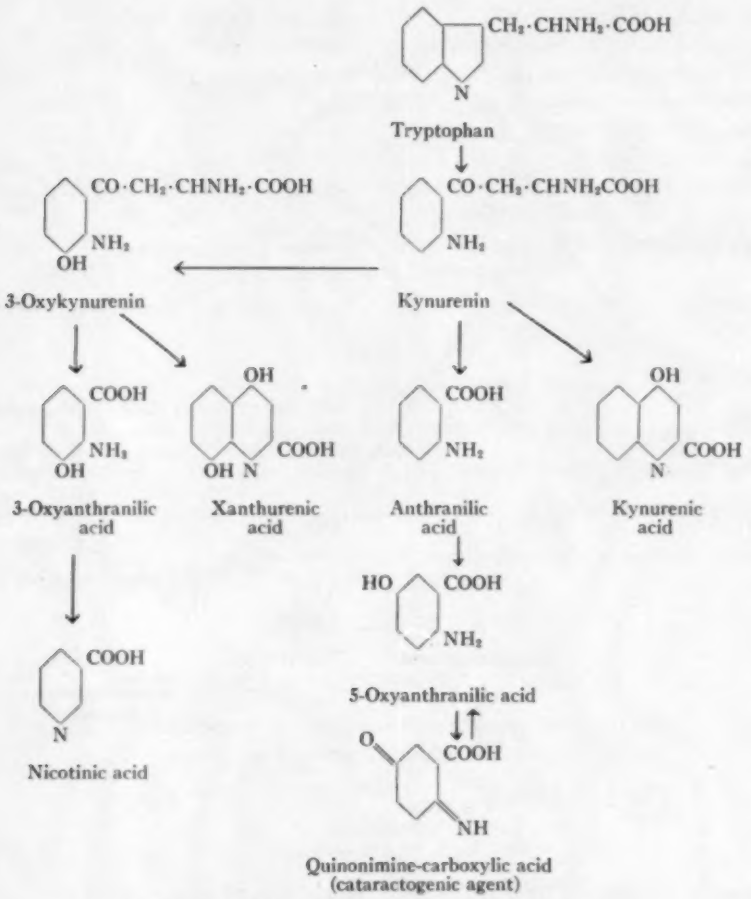

Fig. 2 (Ogino, et al.). Metabolism of tryptophan and cataractogenic metabolites.

In previous reports, Ogino et al.[5] demonstrated that quinonimine-carboxylic acid, one of the metabolites of tryptophan, was excreted in the urine of patients with senile cataracts and that vitamin-C deficient guinea pigs developed cataract following injection of benzoquinone acetic acid. Male white rabbits were used throughout these experiments. Male albino rabbits weighing 2,000 to 3,000 gm. were placed on a diet consisting of 90-percent Tofukasu,* five-percent casein, two-percent butter, three-percent wheat bran, and sufficient vegetables. They were injected with 10 mg. of p-quinonimine-carboxylic acid prepared from 5-oxyanthranilic acid. Eyes were removed for study at three and seven days.

3. *Naphthalene cataracts.*[2] Male albino rabbits weighing about 2,000 gm. received daily one gm. of naphthalene per kg. of body weight. Eyes were enucleated at eight days and later up to mature cataract formation. Further, vitamin-C deficient guinea pigs were injected daily with three mg. of beta-naphthoquinone. Eyes were removed for

*Tofukasu: Tofu is a Japanese food made of the soluble proteins of soya bean. Tofukasu is the insoluble residue.

study at two, three, and five days.

4. *Diabetic cataracts.*[4] Since the onset of alloxan-diabetic cataracts came earlier following administration of tyrosine, with benzoquinone-acetic acid being excreted in the urine, it seemed apparent that the formation of diabetic cataract was closely related to the abnormal metabolism of tyrosine.

After 48 hours' starvation, male albino rats weighing 100 gm. were given intravenous injections of 35 mg. of alloxan. Two days after injection, all animals excreted urine which was found to be three- to four-plus in sugar content.

It was frequently necessary to re-inject animals to sustain a diabetic condition during the incubation period of the cataract. For five days of the experiment, 100 mg. of tyrosine was given daily to diabetic animals. After two weeks 90 percent of the group showed equatorial and posterior subcapsular cataracts. Rats were killed at this period for histologic examination.

5. *Dinitrophenol cataract.* Ogino et al.[6] observed previously that one of the cataractogenic metabolites of dinitrophenol was 2-amino-p-quinonimine. Consequently, in these experiments, vitamin-C deficient guinea pigs were injected daily with two mg. of 2-amino-p-quinonimine prepared from 2,4-diaminophenol. Two weeks later, 100 percent of the group showed equatorial and posterior subcapsular cataracts. Eyes were removed for study at this period.

Results

1. Clinical changes in lens

The cataractous changes noted in vivo are depicted diagrammatically in Figure 3. The chart indicates that the speed of onset and the progress of these cataracts due to various quinoid substances are all similar. The initial changes were usually equatorial, although occasionally vacuoles were first detected in the posterior cortex. They appeared as dark bubbles by ophthalmoscopy and as white spheres by direct slitlamp illumination. With the passage of time these vacuoles increased in number and frequently appeared to migrate toward the posterior horizontal suture. Occasionally vacuoles seemed to migrate toward the anterior pole. Anterior subcapsular and anterior cortical haze and a paraxial ring of posterior cortical vacuoles frequently occurred with further progression of the cataract. Mature cataracts developed within three or four weeks in all cases. With

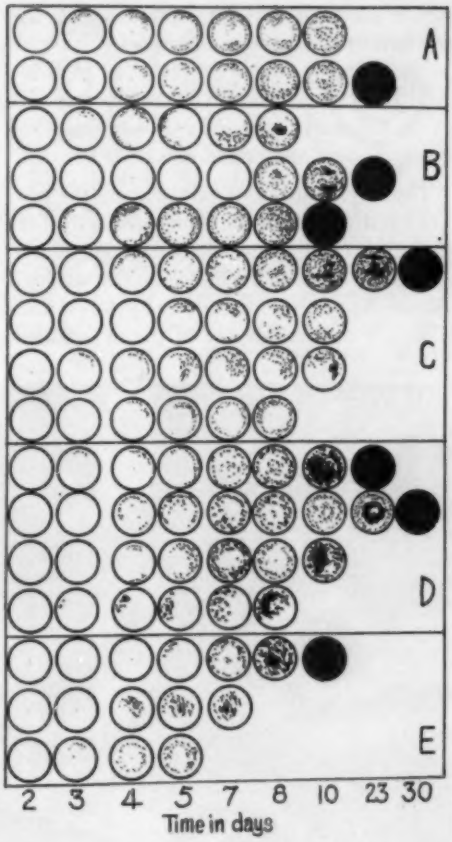

Fig. 3 (Ogino, et al.). Diagram of progression of lens changes in cataract. (A) Cataract in vitamin-C deficient guinea pigs induced by quinonimine-carboxylic acid. (B) Cataract in vitamin-C deficient guinea pigs induced by beta napthoquinone. (C) Cataract in alloxan-diabetic rats administered tyrosine daily. (D) Galactose cataract in vitamin-C deficient guinea pigs administered tyrosine daily. (E) Cataract in vitamin-C deficient guinea pigs induced by 2-amino-p-quinonimine.

higher doses of quinoid substances, similar but more rapid changes occurred.

2. Histologic changes in lens

A. *Cataract induced by quinonimine-carboxylic acid*

The tiny, punctate opacities about the posterior horizontal suture, representing the first clinically recognizable lens change at the early stages, coincided histologically with the appearance of balloon cells and swollen fiber ends. On the second day of the experiment, the anterior capsule of the lens was changed into a wave form, and irregularity and sparsity of nuclei and vacuolar changes in the anterior subcapsular epithelium were observed. In the equatorial subcapsular cortex many small and large vacuoles were demonstrated. In other parts of the cortex there were no changes at this period (fig. 4-A).

In more advanced cataracts on the seventh day of the experiments, the following changes were noted:

Irregularity and sparsity of the nuclei and

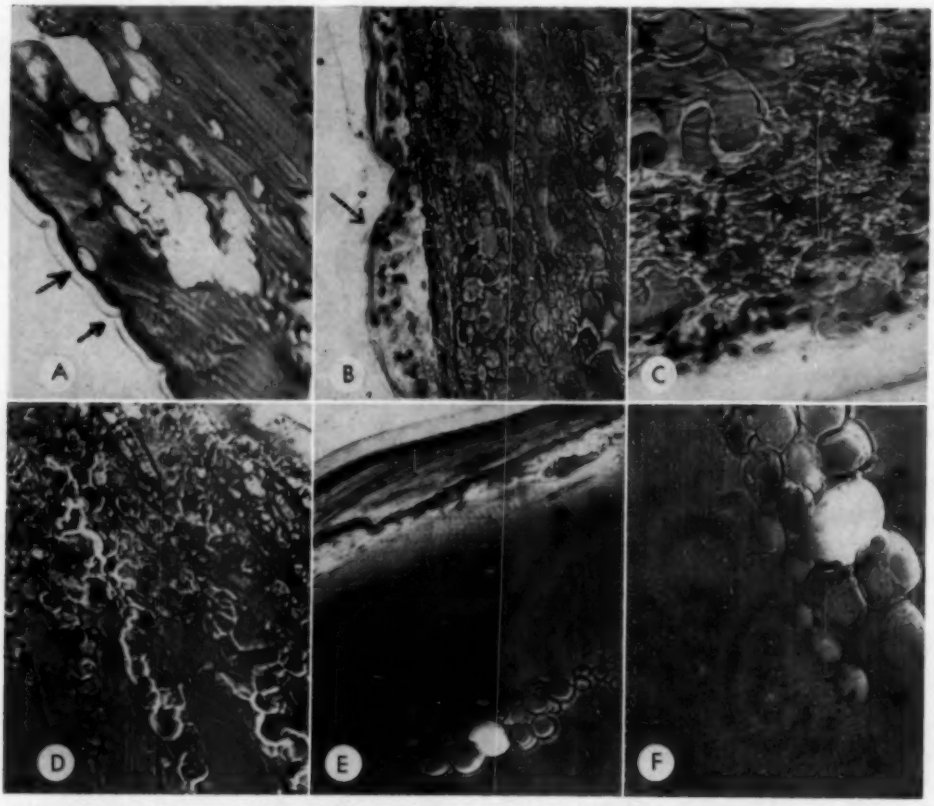

Fig. 4 (Ogino, et al.). (A) Celloidin section of guinea pig lens with quinonimine-carboxylic acid cataract, showing irregularity and sparsity of the nuclei of the anterior subcapsular epithelium and vacuolar changes in the epithelium and equatorial fibers. (B) Cataract seven days after injection, showing hyperplasia of the anterior subcapsular epithelium, irregularity and sparsity of the nuclei, and small and large swollen fibers and vacuoles. (C) Cataract seven days after injection, sectioned through the posterior region, showing pseudo-epithelium in the posterior subcapsular cortex. (D) Cataract seven days after injection, section through posterior region, showing large swollen fibers and a large vacuolated area. (E and F) Cataract seven days after injection, section at the posterior cortex, showing large vacuoles.

vascular changes in the anterior subcapsular epithelium; thinning of the anterior subcapsular epithelium in some instances to such extent that it presented only a fine membrane; proliferation of the anterior subcapsular epithelium in several layers; and breakdown and vacuolar changes of the cortical fibers (fig. 4-B). Occasionally pseudo-epithelium was observed in the posterior subcapsular cortex (fig. 4-C). Breakdown of nucleus to amorphous material was observed in more advanced cataracts (fig. 4-E and F).

B. *Naphthalene cataract*

1. *Changes in the lenses of guinea pigs injected with beta-naphthoquinone.* On the second day of experiments, beginning small hydropic cells were observed as a pale-stained zone in the equatorial region of the lens (fig. 5-A).

On the third day bubbles or vacuoles usually appeared in the subcapsular region near the lens equator. On the fifth day, there were irregularity and sparsity of the nuclei of the anterior subcapsular epithelium and vacuolar changes in the subcapsular epithelium, balloon cells and swollen fibers in the posterior subcapsular cortex, and breakdown of the posterior cortical fibers. (fig. 5-B and C).

2. *Changes in the lenses of rabbits receiving naphthalene.* Incipient cataract ap-

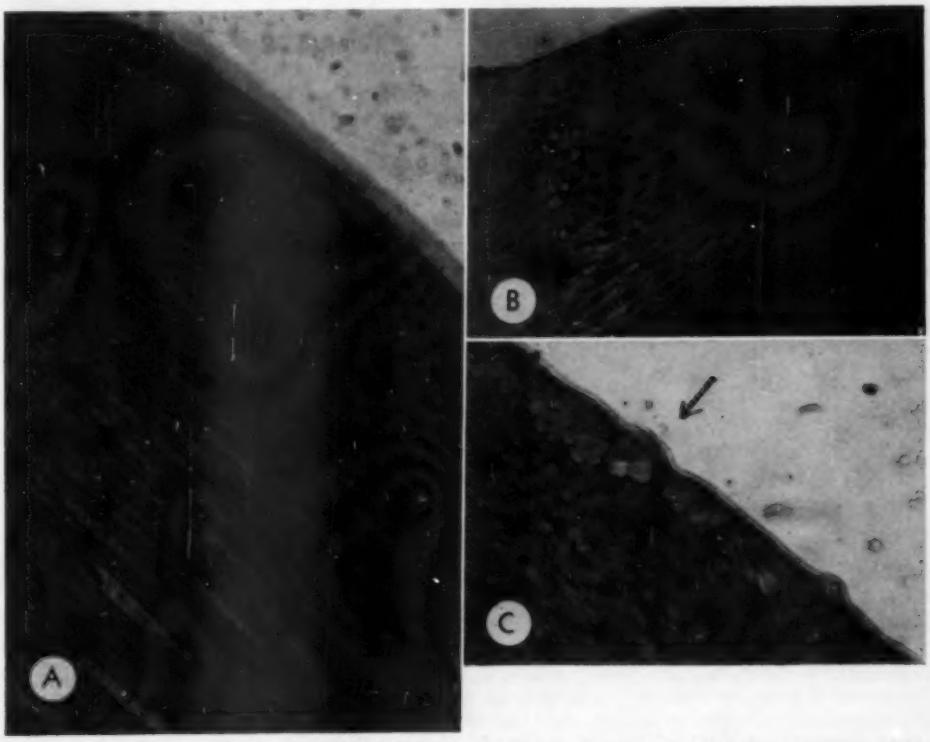

Fig. 5 (Ogino, et al.). (A) Lens of guinea pig injected with beta naphthoquinone two days after beginning of experiment. Sagittal section through the lens bow, stained with hematoxylin-eosin, showing the beginning of hydrops of the lens fibers. (B) Guinea pig lens five days after experiment. Section at equatorial region, showing disarrangement of nuclei with swollen fibers and vacuoles. (C) Guinea pig lens five days after experiment. Section at posterior region, showing granular precipitates beneath the posterior capsule.

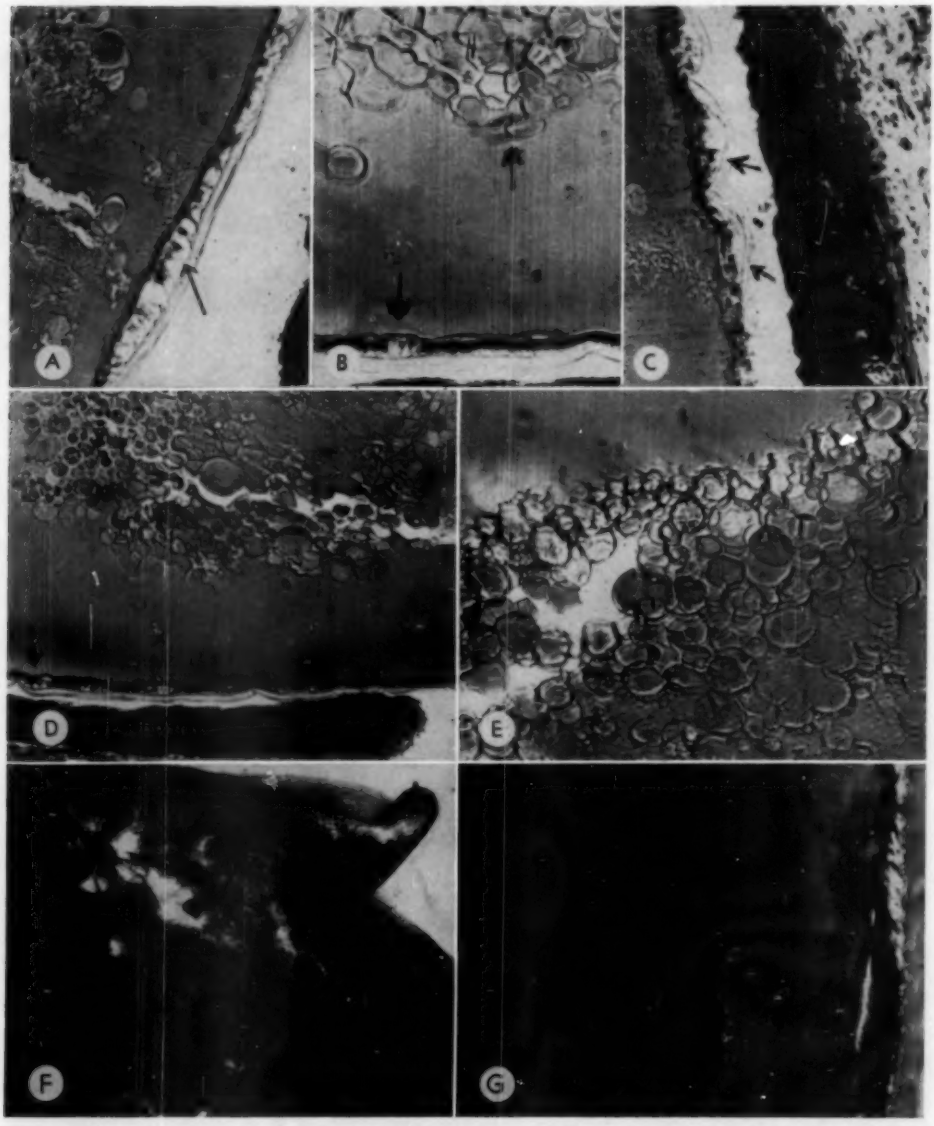

Fig. 6 (Ogino, et al.). (A, B, and C) Incipient cataract in rabbit eye eight days after beginning of experiment. Sections at anterior region, showing marked hyperplasia of epithelium, vacuolar changes in the anterior subcapsular epithelium, and many swollen fibers in the anterior cortex. (D, E, F, and G) Mature cataract in rabbit eye 23 days after beginning of experiment. Section at anterior and posterior cortex, showing initial hyperplasia of subcapsular epithelium and Morgagni's spheres.

peared in the eyes of rabbits receiving naphthalene on the eighth day, with thickening of the anterior capsule, irregularity and breakdown of the nuclei of the subcapsular epithelium, proliferation of the subcapsular epithelium, pseudo-epithelium in the posterior subcapsular cortex, breakdown and vacuolar changes of various parts of the lens cortex

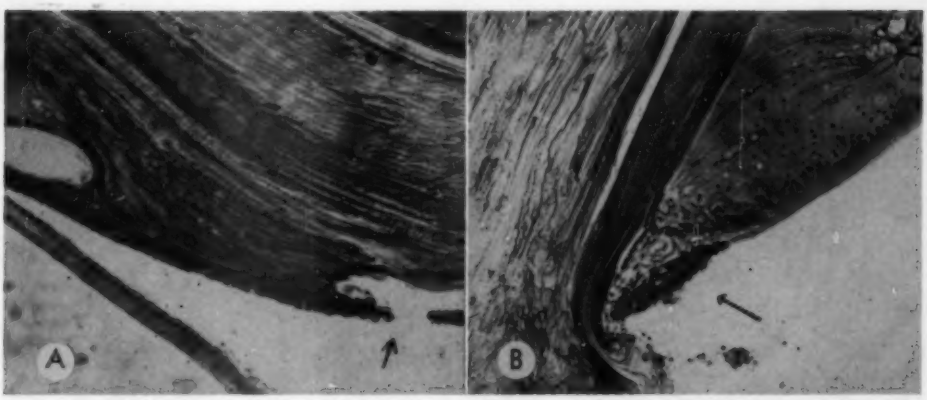

Fig. 7 (Ogino, et al.). (A) Galactose cataract in guinea pigs 10 days after beginning of experiment. Section at anterior region, showing large vacuoles beneath the anterior subcapsular epithelium. (B) Galactose cataract three weeks after beginning of experiment. Section at posterior region, showing marked pseudo-epithelial cells in the posterior subcapsular cortex.

(fig. 6-A, B, and C). In more advanced mature cataracts, such changes as irregularity and breakdown of the nuclei of the epithelium and vacuolar changes of cortex were more severe than in the early stages.

During this period, too, morgagnian globules were usually seen in the anterior and posterior cortex (fig. 6-D, E, F, and G).

C. *Galactose cataract*

The changes in galactose cataracts were similar to those in naphthalene cataract. In all cases, the breakdown and vacuolar changes of the anterior subcapsular epithelium and the breakdown of cortical architecture to amorphous material were observed. Occasionally pseudo-epithelium was seen in the posterior subcapsular cortex (fig. 7-A and B).

D. *Alloxan-diabetic cataract*

In the early stages of these cataracts, small vacuolar changes were observed in the equatorial cortex. In more advanced stages, hyperplasia and breakdown of the anterior subcapsular epithelium, breakdown of cortical fibers, hydropic fibers, many small vacuoles in the anterior and posterior cortex, and swollen nucleated fibers in posterior cortex were observed (Fig. 8-B, C, and D).

E. *Dinitrophenol cataract*

In this cataract, also, the changes were similar to those in the other cataracts described. The breakdown of cortical architecture to an amorphous material and vacuolar changes in the anterior subcapsular epithelium were seen (fig. 9-A, B, C, and D).

3. Histologic changes in other ocular tissues

The changes observed in other ocular tissues, such as iris, ciliary body, and choroid, were similar to those of intoxication. Vascular congestion and round-cell infiltration and degenerative changes were observed.

Slight changes were noted in the periphery of the retina in some of the sections. Atrophy was present in the bacillary layer near the ora serrata. However, that the experimental cataracts were not secondary to these inflammatory changes could be demonstrated in two ways: (1) the inflammatory changes in the various ocular tissues were very slight; (2) in a case in which there were cataractous changes in the right eye and not in the left, the inflammatory changes were the same in both eyes.

Discussion

The histologic pattern revealed by hema-

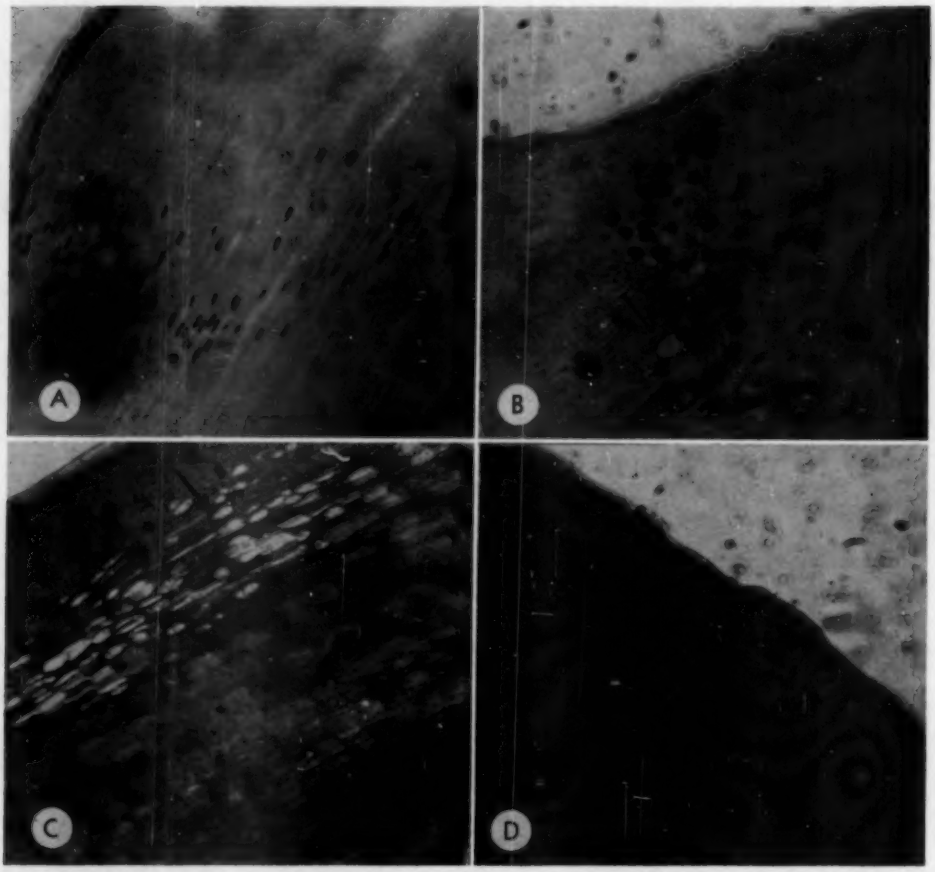

Fig. 8 (Ogino, et al.). (A) Normal control rat lens. Section at equatorial region. (B) Early stage of alloxan-diabetic cataract in rat. Section at equatorial region, showing disarrangement of nuclei and early degeneration of the equatorial fibers, as evidenced by vacuoles and swollen fibers. (C) Anterior section, showing vacuolar changes in the lens fibers. (D) Posterior section, showing destruction and vacuoles in posterior cortex.

toxylin-eosin in various quinoid cataracts does not differ from that in other cataracts previously described by many workers. In all five forms of experimental cataracts hydropic lens fibers are found.

In the earliest stages of the cataracts the hydropic cells were found in a zone somewhat beneath the surface in the equatorial region of the lens. This zone was narrower and more deeply located in the galactose and diabetic cataracts, and more diffuse and more superficial in the quinonimine carboxylic acid cataract. In all five series in animals killed at the time when ophthalmoscopically visible opacities and vacuoles could shortly be expected, but when no opacities were as yet visible, some moderately swollen hydropic cells were found. No similar lesions were found in the control animals.

Consequently, it is concluded that hydrops of the lens fibers represents the earliest recognizable change in the lens cortex in the development of cataracts of the types studied. Rupture and dissolution of the hydropic cells

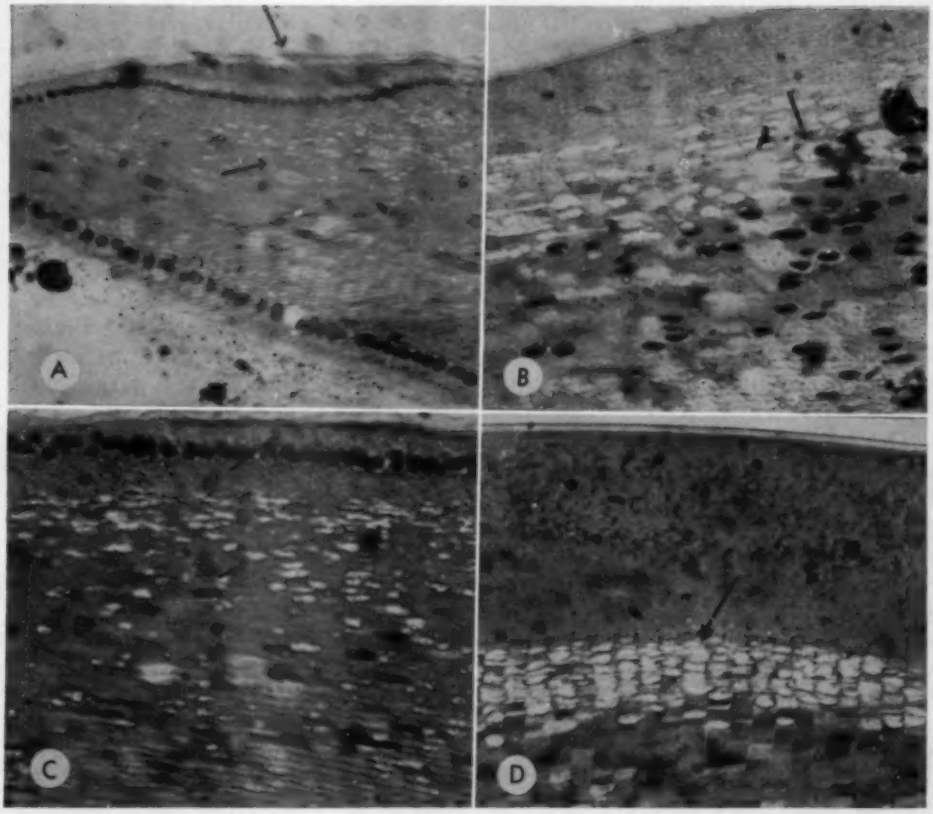

Fig. 9 (Ogino, et al.). (A) Dinitrophenol cataract in guinea pig. Anterior section, showing thickening of the anterior capsule, irregularity of the epithelial nuclei, and vacuolar changes in the cortex. (B) Section at equatorial region, showing vacuoles and nucleated swollen fibers. (C) Section at anterior cortex, showing vacuolar changes in the anterior cortex fibers. (D) Section at posterior cortex, showing breakdown and vacuolar changes in the posterior cortex fibers.

can be seen in the more advanced stages, leading to interfibrillar clefts filled with protein coagulum.

In our study, the clinical appearance of cortical vacuoles was usually accompanied by the histologic picture of balloon cells, although the appearance of vacuoles might also be produced by cystic clefts, as noted by von Sallmann.[7] The balloon cells, called pseudo-epithelial cells by Rohrschneider[8] and "Blasenzellen" (bladder cells) by Krückman,[9] have been further described by Leinfelder and Kerr.[10] Our work supports the belief that they are derived from the developing equatorial fibers.

The chronologic studies described in the present report indicate that the nucleated balloon cells migrate from their site of origin at the equator to the anterior and posterior poles. The clinical progress of the vacuoles is of the same character; therefore, we believe that clinical vacuoles usually result from balloon cells rather than from intracellular hydration phenomena. Their migration seems most probably to be the result of their being crowded away from the equator by newly developed fibers, both normal and pathologic.

Swelling and degenerative changes in the

equatorial subcapsular cells, abnormality and attenuation of the anterior subcapsular epithelium, atrophy of the anterior subcapsular epithelium to a fine membrane, and destruction of the cortical architecture have all been observed in previous studies.

From these results, it is evident that no qualitative differences were noted in respect to the cataractous change in the five types of cataracts. Further, it is of much importance that the findings in the cataract caused by quinonimine-carboxylic acid isolated from the urine of patients with senile cataract are similar to those found in other types of cataracts.

The histologic abnormalities in the various quinoid cataracts may be summarized as follows:

Initially there is a change in the equatorial region consisting of swelling of the fibers and the separation of the fibers by small and large vacuoles. The nuclei of the cells of the growing fibers are disarranged and some nuclei show evidence of degeneration. Some of the swollen fibers beneath the epithelium and also beneath the posterior capsule degenerate.

With more advanced injury, there is further degeneration of the fibers of the cortex, and fragmenting nuclei are found in the anterior or posterior subcapsular region.

In the more advanced cataracts, a granularlike precipitation or morgagnian globules are found either between the epithelium and the capsule, replacing the epithelial cells, or under the posterior capsule. With still more advanced injury the deeper cortical fibers become swollen and vacuolated and have pyknotic nuclei. The earliest change observed in the epithelium was alterations in the nuclei, some of which were pyknotic and others large and pale-staining. In some lenses with still more advanced stages of cataract formation there was hyperplasia of the epithelium.

Our findings regarding the development of the cataracts induced by various quinoid substances are for the most part in accord with those of previous workers in the field.

Summary

A study of the clinical and histologic changes in the cataracts induced by various quinoid substances, such as quinonimine-carboxylic acid, benzoquinone-acetic acid, and 2-amino-p-quinonimine, was described.

The changes noted in these cataracts are similar to those in other cataracts previously reported. In the early stages of cataract, irregularity and sparsity of nuclei of anterior subcapsular epithelium and vacuolar changes in the equatorial cortical fibers are observed. In more advanced cataract, breakdown of the cortical architecture to amorphous material, Morgagni's spheres and vacuoles in the cortical fibers, and pseudo-epithelial cells in the posterior subcapsular cortex are demonstrated. Generally these findings are attributed to the proliferative and degenerative changes in the subcapsular epithelium and cortical fibers. Moreover, there is no marked difference in the changes of cataracts induced by various quinoid substances.

From these results, it is assumed that the characteristics of these various cataractous changes may be attributed to the activities of the cataractogenic agents and to species difference.

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Ophthalmic Miniature

The eye is a rather inefficient organ until it reaches a large size. The back of the human eye on which an image of the outside world is thrown, and which corresponds to the film of a camera, is composed of a mosaic of "rods and cones" whose diameter is little more than a length of an average light wave. Each eye has about half a million, and for two objects to be distinguishable their images must fall on separate rods or cones. It is obvious that with fewer but larger rods and cones we should see less distinctly. If they were twice as broad, two points would have to be twice as far apart before we could distinguish them at a given distance. But if their size were diminished and their number increased we should see no better. For it is impossible to form a definite image smaller than a wavelength of light. Hence a mouse's eye is not a small-scale model of a human eye. Its rods and cones are not much smaller than ours, and therefore there are far fewer of them. A mouse could not distinguish one human face from another six feet away. In order that they should be of any use at all the eyes of small animals have to be much larger in proportion to their bodies than our own. Large animals on the other hand only require relatively small eyes, and those of the whale and elephant are little larger than our own.

J. B. S. Haldane, "On being the right size,"
The World of Mathematics, II, 952,
Edited by J. R. Newman, Simon and Schuster, New York, 1957.

NOTES, CASES, INSTRUMENTS

SPONTANEOUS CYST OF THE IRIS STROMA*

DuPont Guerry, III, M.D.
AND
Herbert Wiesinger, M.D.
Richmond, Virginia

Cysts of the iris stroma occurring without known cause are described in the ophthalmic literature as spontaneous iris cysts. The number of cases reported is surprisingly small, there being a great dearth of histologic data in such cases. Tertsch[1] in 1914 collected 41 cases, the majority of them occurring in individuals under 20 years of age. Since then we have been able to find only one case with a detailed histologic study, that reported by Laval[2] in an individual, aged 57 years, and four clinical cases reported by Marc Amsler[3] and F. Sochor[4] who emphasize the differential diagnosis between cysts and malignant melanoma.

The clinical picture in all reported cases is strikingly similar, consisting of a slowly growing semitransparent vesicle, pigmented or unpigmented, localized usually in the pupillary area. Secondary changes have been rare.

There is considerable disagreement as to the origin of these spontaneous cysts of the iris stroma. Many older writers and some present-day ones consider them mesodermal in origin, their wall being composed of endothelial cells (Boehm,[5] Schmidt-Rimpler,[6] Collins,[7] Juselius[8]). This theory has been opposed by others,[9] particularly Ida Mann,[10] who believes that spontaneous iris cysts may be formed by the neuro-epiderm of the optic cup rim before pigmentation. This would account for the greater number of unpigmented as compared with pigmented cysts. More recently Politzer[11] has reported histologic findings on sections from four human embryos having small vesicles springing from the anterior border of the optic cup. The author thinks it likely that these may contribute to the formation of spontaneous iris cysts.

The case observed by us was that of a three-year-old girl who, while under the constant care of a pediatrician, at the age of three years developed a low degree of esotropia and "a spot on the iris of the left eye not previously noted." She was referred to us for diagnosis and treatment and on the first visit the clinical picture was as follows:

In the 11-o'clock meridan of the left eye a slight brownish translucent cyst could be seen arising from the surface of the iris about one third of the distance from the pupillary margin to the limbus and extending well into the anterior chamber. The cyst did not encroach on the posterior confines of the cornea but when the pupil was dilated, it overlapped the pupillary margin considerably (fig. 1).

Over a period of several months the cyst gradually increased in size, although on one occasion it appeared slightly smaller than on the previous visit, and at that time it was hoped the lesion might spontaneously regress. When this did not occur and the cyst had become large enough to encroach on the undilated pupillary aperture, surgical excision was advised and carried out.

Fig. 1 (Guerry and Wiesinger). The cyst did not encroach on the posterior confines of the cornea but when the pupil was dilated it overlapped the pupillary margin.

* From the Department of Ophthalmology, Medical College of Virginia.

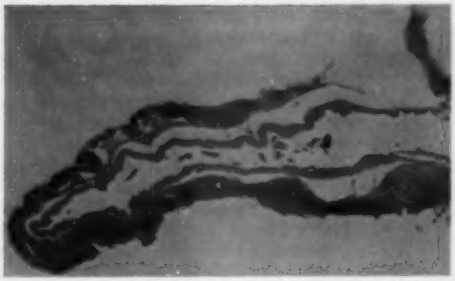

Fig. 2 (Guerry and Wiesinger). Microscopic appearance of cyst.

Through a small keratome incision at the 12-o'clock position, just at the limbus, iris forceps were introduced and the cyst grasped at its peripheral 3-o'clock meridian. It was then pulled slowly into the wound and as much as could be mobilized (about the anterior two thirds) was excised. Following this the pupil assumed its regular round shape and several small, slightly pigmented tags could be seen in the area from which the cyst had sprung. Complete marsupialization of the cyst was thus accomplished and a histologic specimen obtained. Healing was uneventful and after two years' time, there has been no recurrence. The small tags noted immediately after surgery are now completely atrophic and can only be seen with the corneal microscope.

The patient was found to have a mild accommodative esotropia which has been well controlled with +3.0D. sph.

The portion of the cyst excised was found to be lined with a layer of cuboidal cells, as shown in Figure 2. These were partly desquamated into the cyst lumen, either by operative trauma or during preparation. Outside of these cells, the cyst was lined with a homogenous hyaloid capsule. Around the capsule there were pigmented cells of the iris stroma. In the literature available to us we have not been able to find a similar histologic picture of a spontaneous iris cyst showing this peculiar hyaloid membrane.

The microscopic slides were also examined by Dr. Algernon B. Reese of New York and we quote from his report:

"There seems to be a hyaloid capsule which resembles a cuticular product and the inner surface of this is lined with some cells which could be endothelial. Around the capsule are the pigmented cells of the iris stroma. I am not familiar with any lesion of the iris having this structure."

Summary

A three-year-old girl who developed a spontaneous semitransparent iris cyst is presented. The slowly growing cyst produced no symptoms or secondary changes. It was excised partially through a keratome incision and has not recurred. The histologic picture shows a lining of cuboidal cells, probably endothelial, beneath which there is a cuticularlike hyaloid membrane. No similar picture has been found in the literature available to us.

2015 Monument Avenue.

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NYSTATIN IN MONILIA KERATOCONJUNCTIVITIS*

A CASE REPORT

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Prior to the introduction and widespread, and sometimes uncritical, use of antibiotics, fungus infections of the eye were either uncommon or almost always undiagnosed. While there are recent reports in the ophthalmic literature indicating an increasing awareness of the danger of preparing a fertile field for the growth of pathologic fungi in the eye by the topical use of combined antibiotic and steroid therapy, the dangers inherent in the indiscriminate uncontrolled and prolonged use of these therapeutic agents are evidently not too well appreciated.

The following case report is made both to emphasize these dangers and to point out the efficacy in this one case of an antimycotic, Nystatin,† in eradicating the pathologic fungus. Possibly the efficacy of this particular antimycotic for this particular condition is not widely known.

REPORT OF A CASE

The patient, a 66-year-old white man, was seen on July 2, 1956, with a four-week history of a progressive keratoconjunctivitis unresponsive to antibiotic and steroid therapy. There was a strongly positive history of exogenous allergy with asthma and hay fever for a number of years, and also for the past two years during the summer months he had noted itching of both eyes with swelling of the lids and the conjunctivas and injection of the conjunctivas. These symptoms resolved spontaneously around the time of the first frost in the fall. The antibiotic and steroid therapy was originally prescribed to control what was presumed to be an allergic conjunctivitis.

On examination there was marked chemosis and injection of the conjunctivas. The lids were edematous and inflamed. There was a stringy mucopurulent discharge, O.U. The corneal epithelium was roughened and, scattered in the superficial stromal layers, were numerous roughly circular grayish opacities having irregular frayed borders with streamers stretching in all directions. In the left eye in the lower quadrant of the cornea there was a frank open ulcer with a necrotic center (fig. 1).

On examination of the discharge from both eyes no eosinophils or bacteria were found; however, many yeastlike structures were seen. This material was then planted on Sabouraud's media. The patient was placed on an oral antihistiminic, local saline compresses, and sulfisoxazole diethanolamine (Gantrisin) ophthalmic drops as a prophylactic measure. In three days the Sabouraud's media was overgrown with Candida albicans. No clinical improvement was noted. Exogenous iritis developed in the left eye with posterior synechia. These were freed with adrenalin packs.

On July 9, 1956, oral Nystatin (500,000 units, three times daily) was ordered. After two days of this regimen, no improvement was noted and the aqueous flare in the left eye had increased.

Acting on the suggestion of Dr. Susan Dees, Dr. Gavin Hildick-Smith of the Squibb Institute made available experimental ampules of purified Nystatin (Squibb Mycostatin) which had been prepared for intravenous use. A suspension of this purified material in normal saline containing 8,000 units per cc. was prepared and this was instilled in each eye one drop every hour. After three days of this regimen the right eye had cleared markedly with healing of the epithelium. The original corneal ulcer in the left eye also healed; however, other ulcers about the margins of the cornea developed and the aqueous flare increased.

As the solution of Nystatin appeared to be well tolerated, a new solution was prepared with the strength of 20,000 units per cc. and this was in-

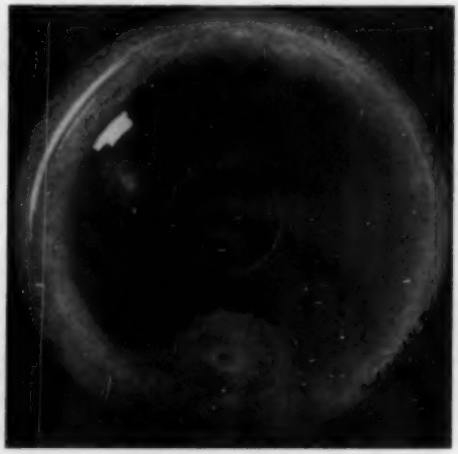

Fig. 1 (Roberts). J. B. (E36206). Keratitis Candida albicans. July 13, 1956.

* From the Division of Ophthalmology, Duke University Medical School.

† Obtained through the courtesy of Gavin Hildick-Smith, M.D., associate medical director, The Squibb Institute for Medical Research, New Brunswick, New Jersey.

stilled as before. Since the iritis appeared to be getting out of hand, it became necessary to take a calculated risk by again resorting to the topical use of cortisone in the left eye. Gradual improvement ensued and on July 18, 1956, all of the ulcers had healed. The patient was discharged on atropine and cortisone topically in the left eye with continued use of Nystatin, O.U.

On return visits, continued improvement of the iritis, O.S., was noted and the lids and the conjunctivas resumed their normal appearance. When the patient was last seen on August 8, 1956, the iritis was completely cleared and there were only residual corneal scars. Cultures of Sabouraud's media taken from the discharge, O.U., were negative 24 hours after beginning the topical Nystatin therapy. Sensitivity studies by Dr. Norman F. Conant of the Department of Bacteriology of Duke Hospital, using the Candida albicans isolated from this patient, showed growth on Sabouraud's agar at a pH of 6.0 when a solution of 25 units of Nystatin per ml. was used but growth was inhibited when a solution of 50 units per ml. was used. On brain-heart infusion agar, pH 7.4, growth occurred when a solution of 12.5 units of Nystatin per ml. was used but was inhibited by a solution of 25 units of Nystatin per ml.

Summary

This is a case of Candida albicans involving the conjunctivas and producing corneal ulceration, the organism probably being a secondary invader following the treatment of allergic conjunctivitis with antibiotic and steroid therapy. The organism responded dramatically to topical Nystatin.

Duke University Medical School.

JIMSON WEED MYDRIASIS IN FARMERS

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The following case reports of Jimson weed mydriasis in farmers are presented to emphasize the importance of this rather common occupational hazard, to point out some of its common features, and to comment on its clinical significance.

Case reports

Case 1

In the fall of 1954, a farmer, P. W., aged 26 years, in otherwise excellent health was seen with unilateral mydriasis of one week's duration. There was no history of injury; vision was normal in both eyes; the left pupil did not respond to light and, in the left eye, there was paralysis of accommodation. Physical examination and laboratory data revealed no abnormality. X-ray studies of the chest were normal. No treatment other than observation was advised and, although the patient was not seen again, it was understood from his employer that the condition cleared spontaneously.

Case 2

This case was likewise in a young healthy farmer, M. A., seen in the fall of 1954. His distance vision was normal, and there was no history of injury. No abnormalities were found by either physical or ocular examination. The patient's only complaint was abnormal light sensitivity. He stated that the sun seemed excessively bright during threshing, at which time the condition was first noted by him. No treatment was advised other than observation and, since he was to return if necessary, it is presumed that he had no further difficulty for he failed to report for further observation.

Case 3

In October, 1955, a similar case was seen in another young adult farmer, H. F. No other abnormalities were found other than the dilated pupil and paralysis of accommodation. Distance vision was normal and the patient was advised to wear dark glasses and to return for observation. Since he did not return, it is presumed that he had no further difficulty.

Case 4

Also in October, 1955, similar findings were observed in a young farmer, J. M., with normal vision. He complained that he was unable to see near objects with the left eye and that dazzling was somewhat disturbing to him. Again examination failed to reveal any other abnormality, and the patient was placed on dark glasses and observation. The condition began to clear in a few days and there was an uneventful recovery.

It is interesting in this particular case that the actual causative agent was discovered by the patient's wife who had found a seed of the Jimson weed in the cul-de-sac of the affected eye. This was considered the cause of the mydriasis.

Comment

In the cases considered, there was no history of trauma, and the unilateral mydriasis was of the paralytic type rather than irritative. The vision, as noted, was normal for distance in each case, although there was difficulty with near vision. Intraocular pressure in these mydriatic eyes was normal, although it is to be noted that all of the farm-

ers involved in the four cases reported here were young. The clinical implications of the same occupational hazard occurring in older individuals are obvious. Certainly all individuals, particularly those with a predisposition to glaucoma, should exercise considerable care while engaged in harvesting activities, in order to avoid the possibility of precipitating an attack of mydriatic, closed-angle glaucoma.

It would seem to be advisable also for ophthalmologists and other physicians to keep this rather simple explanation of a suddenly occurring unilateral mydriasis in mind, so that it can be properly evaluated in its true relation to other and sometimes much more serious conditions which should be included in the differential diagnosis. For farmers who have recently been working with a corn picker or combine, the Jimson weed should be suspected as a likely cause of a suddenly appearing unilateral mydriasis. It is conceivable that this suspicion plus a careful history might avoid many unnecessarily extensive neurologic, roentgenologic, and laboratory investigations. A short waiting period of two to three weeks, with no further exposure to Jimson weed, will clarify the diagnosis.

Jimson weed mydriasis may be more common than is realized, since it is possible, because of the transient nature of the mydriasis, that the condition may often go unrecognized.

The active ingredients of Jimson weed are stramonium and hyoscine (scopolamine). They are found in the dried leaf and flowering or fruiting tops, with its branches, of Datura stramonium linne or of Tatula (linne) torrey (fam. Solanaceae).*

It is well known that Jimson-weed poisoning is not uncommon among children living in suburban or rural areas. This poisoning, however, is due to ingestion which results in constitutional symptoms, such as skin flushing, tachycardia, dry mouth, excitement, irritability, fever, and convulsions, together with mydriasis, which is of course bilateral, instead of unilateral as in the cases reported here.

* National Formulary. Easton, Pennsylvania, Mack Co., 1955, ed. 10. Also in U. S. Dispensatory, p. 1172.

Summary

Four cases of transient, unilateral mydriasis in young healthy farmers are reported. All occurred in the fall of the year during harvesting activities. In one of these cases a seed from the Jimson weed was actually found in the cul-de-sac of the affected eye. In these young individuals the intraocular pressure was unaffected by this mydriasis but the possibility of the weed precipitating a mydriatic glaucoma in more susceptible individuals should be emphasized. Jimson-weed poisoning is presumed to be a rather common occupational hazard of farmers but, because of its transient nature, unilateral mydriasis due to Jimson weed probably occurs much more frequently than it is recognized.

525 Glass Block.

TRANSIENT LOSS OF VISION FOLLOWING USE OF QUININE*

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New York

Quinine, derived from cinchona, is used for malaria and the common cold. Quinine poisoning is not very common, occurring in 1/100,000 persons susceptible to this drug. Women and children are most susceptible. The average dose is 5.0 to 10 gr., yet cases of toxic visual symptoms have been reported from 1.0 gr., although 30 to 60 gr. taken throughout a day caused transient loss of vision. The symptoms are usually bilateral, acute, and sudden in onset. Visual failure may be complete, with total loss of light perception, like a shutter drawn across the eyes, or loss of vision may not occur for days or weeks. Cases of optic nerve atrophy with permanent loss of vision, though extremely

* From the New York Medical College.

rare, have been reported. There is, however, a tendency to recover.

Pathology. There is a degeneration of the ganglion cells with an ascending type of optic-nerve atrophy. This is accompanied by narrowing of the retinal arteries.

Symptoms. Blindness may be complete, partial, or transitory, lasting several days or months, and may be accompanied by flashes of light and visual hallucinations. There is flushing of the face, dilated pupils, which do not react to light, fullness of the head, ringing of the ears, and deafness. Cases of delirium and convulsions, have been reported. Death in coma and status epilepticus have also been described.

Bishay reported that the onset of quinine amblyopia could be very rapid, with blanching of the conjunctivas and anesthesia of the cornea, with early loss of fields for red and blue. In recovery the fields for red and blue are reversed, with a relative loss for blue.

Ophthalmoscopic studies reveal haziness of the disc margins with some pallor of the surrounding retina. The retinal arteries are constricted and the appearance of the fundi simulates obstruction of the central retinal artery, following the use of quinine within 15 hours. Oddly, as vision returns, the arteries become increasingly narrow and the discs become increasingly pale but the disc margins are well defined.

There is frequently seen brownish specks in the macula—comparable to the cherry-red spot in Tay-Sachs' disease. These brownish specks in the macula gradually disappear. Abadie believes the macular changes seen in quinine poisoning are due to a generalized narrowing of the arterial system or to a spasm of the central retinal artery, whereas in amaurotic family idiocy, the cherry-red spot in the macula remains to the end.

There is concentric contraction of the fields. Knapp reported that the contraction of the fields may be greatest in the vertical diameter. Central vision improves first and recovery may take days or months.

Biopsy in dogs revealed a degeneration of the ganglion cells and nerve fibers. The walls of the blood vessels were thickened with obliteration of the lumen. In all probability, quinine acts directly on the nervous element and precedes any vascular changes.

Treatment. Discontinuance of the drug is the first step. Such vasodilators as amyl nitrate have been used, as have injections of atropine. Elliott, in 1909, tried paracentesis of the anterior chamber. Trephination has also been tried. Alt, in 1927, found improvement after lumbar puncture.

Case report

Mr. A. T., aged 43 years, a chef, consulted me in November, 1954, with a history of blurring of vision following the use of 5.0 gr. of quinine sulfate three times a day for two days for a common cold.

An examination revealed a well-nourished male, short and stocky, with a florid complexion. His visual acuity was 18/200 in the right eye and light perception in the left eye. He claimed his vision was excellent prior to the use of quinine. His past history was irrelevant.

Eye examination revealed a chronic folliculosis. The muscles had motility in all directions. There was a small macula of the right cornea at the limbus at the 2-o'clock position which was the result of a burn from a hot cinder many years ago. The fundi revealed slight pallor of the discs, and the adjacent arterioles were moderately constricted. In the left fundus above the macula there was an area of choroidal atrophy. Field studies showed concentric contraction more marked for blue. There was also a paracentral scotoma in the right eye. Tension was well within normal limits.

Nitroscleran (0.1 mg.) was given intravenously for 12 days. Vision gradually improved during that time and returned to 20/30 in the right eye and 20/25 in the left eye at the end of two weeks. The appearance of the fundi remained unchanged. The discs were pale and the retinal vessels were still attenuated. The fields were improved.

SUMMARY

A case of quinine poisoning with loss of vision followed the use of 30 gr. of quinine sulfate in 48 hours. Vision returned to normal at the end of two weeks following the use of vasodilators, even though the appearance of the fundi remained unchanged.

525 Park Avenue.

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EPIBLEPHARON AND CONGENITAL ENTROPION*

JESSE M. LEVITT, M.D.
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Epiblepharon and entropion are lid anomalies that may cause lacrimation in infants.

Epiblepharon refers to a fold of skin running horizontally across the upper or lower lid, generally the latter. It is not unusual, and would require little notice but for the fact that in some cases it may invert the eyelashes against the cornea, especially on downward gaze.

Swan recently observed that infants with marked epiblepharon typically have a narrow interpupillary distance, epicanthus, chubby cheeks, and relatively prominent eyes. He reported four cases of epiblepharon associated with a unilateral insufficiency of the inferior oblique muscle, with inversion of the lashes, keratitis, and spastic entropion.

Epiblepharon does not require any treatment unless the cilia rub against the cornea. In that case, adhesive or cellophane tape may be applied to the cheek to pull the skin fold away from the eyeball, or collodion may be used two or three mm. below the eyelash line every few days. In most cases, with the growth and development of the facial bones and the changing elasticity of the skin, the epiblepharon disappears within a year or two, and the lashes assume a normal position.

The following case illustrates epiblepharon with inverted cilia that irritate the corneas.

J. Z., a five-month-old male infant, was brought to my office on March 24, 1955, with a history of tearing of both eyes since two months of age. A pediatrician had suggested that the baby might have trouble with the tear canals.

Examination disclosed bilateral epicanthus and epiblepharon of lower lids, with inversion of the lashes (fig. 1), increased on downward gaze (fig. 2). The lid margins appeared in normal relationship to the globes. The mother was shown how to apply adhesive strips to the cheeks.

Fig. 1 (Levitt). Five-month-old infant, showing epicanthus and epiblepharon of the lower lids, with inversion of the cilia.

Fig. 2 (Levitt). Same child, showing inversion of eyelashes increased on downward gaze.

*From the Brooklyn Eye and Ear Hospital. Presented before the Brooklyn Ophthalmological Society, December 20, 1956.

Fig. 3 (Levitt). Same child at the age of two years, with eyelash lines in normal position.

When the baby reached the age of a year, the eyelashes were in normal position and the epiblepharon, although still present, was not as noticeable. A picture taken on December 1, 1956, when the child was just over two years of age, shows the eyelash line in normal position (fig. 3). The child does not have any paresis of the inferior oblique muscle.

Congenital entropion, which is relatively rare, is sometimes associated with epiblepharon and epicanthus and other congenital anomalies. Most cases are attributed to hypertrophy of the marginal portion of the orbicularis muscle, and a few to absence of the tarsus. The rubbing of the lashes against the cornea may be quite distressing, making surgery imperative at an early age. A simple excision of skin (Celsus operation), may suffice to correct the condition. If operation is postponed to a later age, excision of skin and orbicularis may be necessary.

An example of congenital entropion is the case of C. R., Jr., an 11-month-old male infant, brought to the Brooklyn Eye and Ear Hospital Eye Clinic on October 15, 1956. The mother stated that when the baby was six weeks old, the eyelashes were growing upward and the eyes started tearing, and that the condition kept getting worse.

Examination of the lower lids showed a true bilateral entropion, with the lashes obviously rubbing the corneas (fig. 4). Preoperative study, under general anesthesia, revealed primary inversion of the lid margins, excluding muscle spasm as the cause (fig. 5).

A semilunar fold of skin was resected from each lower lid on November 9, 1956. On the sixth day the sutures were removed. A picture taken four weeks after operation shows the lids in normal position (fig. 6).

Fig. 4 (Levitt). Eleven-month-old child, showing bilateral primary entropion of the lower lids.

Fig. 5 (Levitt). Same child under anesthesia, showing marked inversion of lid margins.

Fig. 6 (Levitt). Same child four weeks after operation, showing eyelids in normal position.

Summary

Epiblepharon and entropion may cause lacrimation in infants. Epiblepharon is relatively common, and may occasionally distort the lash line; it tends to disappear with growth of the face. Congenital entropion, rather rare, causes a permanent inversion of the lashes, requiring early surgical correction. A case of each is presented.

515 Ocean Avenue (26).

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SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

433rd meeting
December 19, 1956

DR. EDWARD A. CRAMTON, *presiding*

PREOPERATIVE CARE AND TECHNIQUE OF RETINAL DETACHMENT SURGERY

DR. ICHIRO D. OKAMURA (Boston, Massachusetts): In 1919 Gonin stated that the fundamental principle of retinal detachment surgery was to close off all the breaks. Coupled with this is the important task of localizing accurately and preoperatively all the breaks and plotting their positions on a chart.

There are two obvious ways of closing off the retinal breaks. The first is to surround the break with diathermy. The method is a matter of choice: surface diathermy, pins, or chemical means. The second method is to wall off the affected area of the retina by means of a barrage. The first method has been found useful for small breaks. The second method, the barrage, is quite effective in cases of large breaks or multiple breaks.

We use the scleral buckling procedure because we found that in many cases the retina did not flatten down in contact with the choroid when the subretinal fluid was removed. Also in some cases when good contact had been achieved some sort of traction, possibly vitreous traction, caused either a return of the break or produced a second tear along the edge of the break.

To push the choroid against the retina we use polyethylene. This is an inert, satisfactory foreign body to use.

The operative procedure developed last and the one we use most frequently is the one with the circling tube. In this operation the conjunctiva is incised 8.0 to 10 mm. from the limbus; Tenon's capsule is separated from the globe; and one to four of the rectus muscles detached. When the sclera is exposed all the breaks are accurately localized. This is done by the surgeon viewing the fundus and the assistant placing the surface electrode along the edge of the break.

The next step is to resect a strip of sclera 3.0 to 5.0 mm. wide. The maximum length is usually three fourths of the circumference of the globe. The resection is so placed that the break will be on the anterior slope of the buckle. The sclera is so removed that the remaining sclera is of uniform thickness. This is done so that the diathermy using a needle applicator can be applied uniformly.

After the application of the diathermy mattress sutures of 4-0 black silk braided are placed. The polyethylene tube, 1.25 mm. in diameter and threaded with 2-0 black silk suture, is passed under the mattress sutures and the uncut rectus muscles. Now the sclera is incised down until the choroid is exposed. The perforation is made in the choroid itself and under direct observation. The subretinal fluid is released. When this had been evacuated the polyethylene tube which may be too long is cut to the correct length. One end of the tube is flapped and split and the other end inserted into it. The mattress sutures are tied and the suture in the tube is tied.

The indications for this procedure are any signs of vitreous traction such as fixed folds, star-shaped folds, multiple breaks, and breaks with rolled up edges. In short, anything that gives the case a bad prognosis.

The second procedure used is the partial tube scleral buckling. This is essentially the same as the first procedure except that, as the name indicates, the tube does not encircle the globe.

The indications for this procedure are insufficient subretinal fluid and a retinal break

that is placed in an extreme posterior position.

The third procedure is the scleral buckling without excision. The break is localized as in the first two procedures and it is then surrounded with partial perforating or surface diathermy using a needle applicator. After the diathermy a scratch incision is made and mattress sutures are placed. After perforation and the placement of two mattress sutures a small length of polyethylene tube is placed under the sutures. The sutures are then tied and an anchoring suture placed. The type of elevation produced in the fundus by this type of operation is not as permanent as that produced by the first procedure.

The indication for this operation is those cases with a macular hole. It is difficult to excise any amount of sclera in these cases.

Question: What do you mean by sufficient subretinal fluid?

Answer: When I say insufficient or sufficient subretinal fluid I am using relative terms. It is hard to describe. The understanding comes only with experience.

Question: What is your reaction to using a strip of sclera and buckling over that?

Answer: We want something solid for the sutures. Sclera is soft, it isn't permanent, it becomes necrotic, and it is necessary to use more sutures with it.

Question: Why do a partial resection? Why not apply diathermy to a full scleral thickness and then put the tube in?

Answer: The thickness of the sclera varies around the circumference of the globe. This variation complicates matters when diathermy is applied. If the sclera is of the same thickness it is possible to apply diathermy uniformly and it is also possible to apply the minimum of diathermy. This is desirable.

Question: Describe your technique in releasing subretinal fluid, particularly those cases that are stubborn.

Answer: If one perforation is made and fluid is not obtained then another perforation is made. It is most important to get the fluid out so the retina is placed in contact with the choroid. Sometimes when a perforation is done the fluid that comes out is thick and clear. This is not necessarily vitreous, it may be fluid that has been there a long time and has a high protein content and is thick. If you perforate and get thick fluid then look at the fundus and see if the retina has been incarcerated by the perforation. If not, then continue to release the thick fluid. If the retina has been incarcerated by the perforation the area should be closed as soon as possible to prevent the loss of vitreous.

Postoperative Care and Complications of Retinal Detachment Surgery

Dr. Charles L. Schepens (Boston, Massachusetts): Any changes we have made in the procedures of retinal detachment surgery were made with the idea of doing in a less traumatic way what Gonin was trying to do. That is, to close adequately and permanently the retinal break. No procedure is 100 percent successful and I am going to speak on the difficulties and complications we run into with the scleral buckling operation.

When the scleral incision has been made too deep the pressure of the needle for the mattress sutures may cause a sudden hernia. This is handled by placing a thin sheet of polyethylene, cut to size, over the area. The needle is then inserted parallel to the incision and the sutures go over the sheet of polyethylene. This prevents pressure on the globe and prevents a bigger hernia of the choroid.

Should this complication of a hernia arise where the sclera is weak or where it had been treated previously by diathermy, a suture is placed parallel to the long axis of the hernia. Once the suture is in place, a thin sheet of polyethylene, cut to size, is placed under the suture and the suture tied as tightly as possible. This can be done only if the eye is soft. To soften the eye either release subretinal fluid or do a paracentesis.

Trouble occurs when the sutures are placed. In those areas of the sclera that are thin or have been treated with diathermy before you tie the suture, slide a small piece

of notched polyethylene under them, and then tie.

Another problem in retinal detachment surgery is the vortex veins. Usually there are four of these although at times there may be six or seven. It is absolutely essential to treat them with as much respect as possible. Nine out of 10 intraocular hemorrhages that occur in retinal detachment surgery are due to an interference with the vortex veins.

When the vortex vein runs right in the posterior portion of the excision we do not deviate from the plane of the excision. We leave the vein alone and make that portion of the excision more shallow. The incision is made deep enough so the veins can be seen. Diathermy is not put on their course. Should it be necessary to sever a vortex vein do it by leaving a stump of about 4.0 to 5.0 mm. and tie both ends. This will prevent the vein from retracting into the globe. On some occasions the vein is gently retracted, the sclera cut from under it and around it, and the polyethylene tube passed under the vein. Should the vortex vein be cut we generally allow it to bleed, we do not cauterize it. The bleeding may be temporary and the wall of the vein will repair itself in time. Also a cauterized bleeding vortex vein may start bleeding on the inside of the globe.

Many complications occur with repeated diathermy operations. One of these is the inability to close the conjunctival wound adequately because there isn't enough conjunctiva left. It is important to have adequate coverage by the conjunctiva and to leave none of Tenon's capsule exposed.

The biggest complication is failure of the operation. When this happens in the scleral buckling procedure the first thing to look for is the presence of retinal breaks on the disc side of the buckle. The cause of failure may be that the buckle was not placed posterior enough. In such cases a reoperation is done, more subretinal fluid is released, and the tube is shortened. The breaks are not treated with diathermy. In extreme cases where there are fixed folds and several breaks on the disc side of the buckle, then a second circling tube is used. The first tube is not removed. An eye that tolerates one tube well will tolerate a second tube.

When a cellular membrane is present in the globe and it causes a detachment, postoperatively this same membrane could pull the retina across the border of the disc and cause a recurrence of the detachment. Sometimes this is curable by reoperation and sometimes it is not. Success depends on the amount of traction the membrane has and its location.

Intraocular hemorrhage is another big enemy. Vitreous hemorrhage is often due to interference with the vortex veins. It is essential never to cut or prick any part of the choroid without actually looking at it. If there is a red streak, extend the section until the choroid is of even color. The brutal release of subretinal fluid through a too large hole may also cause intraocular hemorrhage. The release must be gradual.

Hemorrhages are generally subchoroidal. Leave choroidal detachments alone until four to seven days postoperative. If they are moderate in size they need not be treated. If they are large, a posterior sclerotomy should be done. This should be done carefully. Do not try to remove every drop of fluid or a fresh hemorrhage will start. About one third of the fluid is enough to remove.

The most dangerous type of hemorrhage is that of the ciliary body. If they are severe the patient will have glaucoma, anterior and posterior cortical opacities, and often cataract, and soon, phthisis.

I think that damage to the ciliary body also leads to some form of keratopathy. There are conjunctival edema, swelling of the cornea, bullous keratopathy, a vascularized and often opaque cornea. This is a very mysterious condition to me.

The two foreign bodies, silk sutures and polyethylene tubing, may play tricks on us. For instance they may become exposed. The silk may come through the conjunctiva. Chronic infection sets in and a fistula or abscess will form. These sutures must come out. But be certain of the nature of the

sutures. If the suture is a circling one it should not be cut unless it is infected. Open the abscess, drain it, and insert a fine polyethylene tube; inject bacteriostatic mixture until the inflammation dies down.

A circling tube will not erode through the conjunctiva, but an incomplete tube may. Don't pull one of the tubes out unless you are very certain it is entirely loose. It is often better to incise the conjunctiva and rebury the tube. All tubes should be buried adequately at time of operation. Do not have the tube too long so that it cannot be completely covered.

The last complication is that of sympathetic ophthalmia. Out of 1,800 cases of scleral buckling we have had one case of sympathetic. I have had one case following a straight diathermy operation and one case following lamellar scleral resection without a polyethylene tube. The condition is rare, but it does exist and should be kept in mind.

All these complications should incite us to be more gentle with the eyes we treat. Many complications can be avoided if care and reflection are taken by the surgeon at each step of the operation. On the whole I think the picture is encouraging because the number of successes is overwhelmingly greater than the number of complications or eyes lost.

Question: Will you comment on the appearance of squint following scleral buckling?

Answer: Squint does occur at times. The extraocular muscles become adherent to the spot on the sclera that was handled. It is important to reset the muscles over the area where a large buckling was done. Just how much to reset we learn by experience. Those cases that do not straighten out after six months are operated on. A word of caution, these are not simple squint operations. The scar tissue and the adhesions make them difficult to handle.

Question: Will you describe in some detail the reoperation for a buckle that is too far anteriorly?

Answer: As far as reoperation is concerned, I just hate to unearth a tube that is securely buried. I have had so much trouble with buried tubes that I don't touch them anymore. If a tube is not posterior enough I forget all about it and put another tube in.

Question: How about the refraction in these eyes?

Answer: That is a very interesting thing and I cannot give you a very good answer. Except in the early stages you get a marked increase of the hyperopia and a dimunition of the myopia. As the eye goes on the pressure inside the eye tends to push it back just where it was. You do not change permanently the length of the eyeball as much as you would think. However, if you draw a narrow, high buckle then you often get a marked astigmatism. But even this does not stay for too long.

Question: What are your objections to doing a posterior sclerotomy say about 7.0 mm. back of the limbus to soften the eye rather than doing a paracentesis?

Answer: I think that is about the worst thing that can be done. That is the area of the pars plana where the vitreous base is. The vitreous here is a gel with a high collagen content. Any fluid taken from here would be very thick. Damage would be done to the periphery of the retina. Also you have to make a fairly large hole to get the fluid out and then you would get an ingrowth from the episcleral tissue. There are too many dangers attached to this whole procedure.

Question: How do you sterilize your polyethylene tubes?

Answer: We used to place them in a sterilizing solution. We now have an arrangement with the hospital pharmacy where they do it for us with ethylene oxide. This is a good agent but it is explosive in some mixtures with air and cannot be used in the ordinary operating room set-up. We get them in a little plastic bag all sterile and ready to use.

Charles Snyder,
Recorder.

YALE UNIVERSITY CLINICAL CONFERENCES

February 10, 1956

DR. R. M. FASANELLA, *presiding*

THROMBOSIS OF RETINAL VEIN

DR. BERNARD ROBERTS limited his discussion of ocular pathology in this field to several interesting conditions. He first discussed thrombosis of the central retinal vein. In his opinion a better term would be endophlebitis obliterans. He noted that, except for injuries and tumors, more eyes were enucleated for this condition in the elderly person than for any other. Only if the main vein is involved does hemorrhagic glaucoma occur. Usually the tension is low originally and three months later glaucoma may develop.

Dr. Roberts showed several color slides which demonstrated the various pathologic features in this condition. The iris was noted to be flattened and there were peripheral anterior synechias. There was choroidal engorgement in the optic nerve area. An increase was noted in the glial elements in the papilla, which, according to Dr. Roberts, may be the reason why deep cupping does not develop in this condition despite the glaucoma. This increase of glial tissue in the papilla is produced by an exudative process in the early phases.

The choroidal vessel engorgement in the posterior segment is a compensatory attempt on the part of the circulation to furnish blood to the affected area. Not all cases of central closure develop glaucoma and several theories have been suggested for this.

One theory was that glaucoma developed because of blood stasis, but this doesn't seem likely since glaucoma doesn't occur in the original stages as you would expect, but later.

Another theory mentioned was that the enlarged vitreous body thrust the lens and iris forward. This, however, doesn't seem to happen pathologically.

A third theory was that certain toxins were liberated to cause the anterior segment damage. In the posterior segment, the optic nerve may be the exit pathway for lens and ocular fluids. Increased gliosis may prevent this.

If the collateral circulation of the choroid is adequate, no glaucoma would develop. If inadequate, changes begin in the anterior segment. It is noted that peripheral anterior synechias in this condition are vascularized, a fact which is important in the outcome of the eye. The normal iris folds and crypts and vasculature are lost. A thin membrane is noted on the iris surface with many fine capillaries. This arises from the greater arterial circle and the vessels invade the iris and the angle. Bridge synechias may form. When the tension goes up, the angle may spread and rupture the fine vessels which already have been formed. Likewise, any operation through the angle may lead to further hemorrhage because of these fine bridge vessels. Treatment by cyclodiathermy would probably be better. These points were demonstrated by several beautiful color slides.

ENDOPHTHALMITIS PHACOANAPHYLACTICA

The second condition discussed by Dr. Roberts was endophthalmitis phacoanaphylactica. This is considered to be an ocular reaction to lens material. Possibly the conditions should be called endophthalmitis phacogenica, since it is not a true anaphylaxis. Very little has been written in the literature concerning this condition. Several theories previously advanced include the following:

1. Patient is said to be sensitive to lens material.

2. It has also been theorized that the lens produces a toxin.

3. It has been theorized that this condition is a mild precursor of sympathetic ophthalmia.

Pathologically, the anterior segment is the only part of the eye involved, which is distinctively different from conditions noted in sympathetic ophthalmia. In connection with the toxin theory, it can be noted pathologically that the reaction originates at the lens

with numerous polys surrounding the immediate area of the lens while farther away there are lymphocytes, giant cells, and endothelioid cells. When the second eye becomes inflamed, this may be spontaneous by lysis through the capsule or secondary to an extracapsular extraction in the second eye.

Clinically, Dr. Roberts noted that when the lens capsule is ruptured following extraction and a persistent inflammation develops, this suggests lens sensitivity and the lens should be washed out thoroughly. If further operation is necessary on the second eye, every effort should be made to do an intracapsular extraction.

The value of desensitization or testing by intradermal cysteine was discussed. Dr. Roberts mentioned some data accumulated by workers in India, who noted that in 50 cysteine sensitive cases, those which had extracapsular cataract extraction developed severe inflammatory reactions, whereas of those with an intracapsular only one of 25 had inflammatory reactions. In a second series of 50 noncysteine-sensitive cases no reactions were noted in either group except one of the extracapsular operations.

In summary, Dr. Roberts believed that this is probably a protein sensitivity and suggested that in cases of trauma or where an extracapsular extraction is planned, one should think of this condition.

Hyperplasia of pigment epithelium

A third subject brought up by Dr. Roberts was illustrated by a case of a 20-year-old boy, who had an enucleation for a small presumptive malignant melanoma near the disc. Pathologically, this turned out to be hyperplasia of the pigmentary epithelium with some fibrous metaplasia in the juxtapapillary area. The pigmentary epithelium demonstrated proliferation, migration, and fragmentation. Dr. Roberts has had experience with five such cases all in exactly the same location.

The exact nature of this condition is unknown but the practical importance was noted of distinguishing this from small malignant melanomas and Dr. Roberts suggested that one should be very conservative about removal of an eye with good vision, where the tiny melanotic lesion is adjacent to the disc.

Glaucoma capsulare

A fourth condition discussed was so-called glaucoma capsulare caused by exfoliation of the lens capsule. Dr. Roberts is not convinced of the correct diagnosis of exfoliation. To his mind it seems to be a collection of granular material resting on the lens capsule. Similar collections were noted in the posterior iris folds and in the ciliary processes. There is some pigment involved which does not come from the lens. In the angle meshwork was a similar granular material and pigment obstructing the meshwork. Not all of these cases developed glaucoma, depending chiefly on the quantity of involvement. However, 60 to 70 percent do get glaucoma. Dr. Roberts does not believe the lens is responsible but feels that something in the senile eye is causing these extrusions of granular material and mechanical angle obstruction.

Discussion. Dr. Freeman: The pathology of the veins in general is poorly understood. The choroidal vessels around the disc in general do not drain the retina. Many thrombosed retinal veins show recanalization. Pigment epithelium is derived from the neural crest and is truly a neural tissue. In the eye it does not react as a true epithelial tissue and at present there is still not too much known about its exact behavior.

Dr. Rosenthal: I have noted that in diabetes one often sees a rubeosis of the iris without any thrombosis. Likewise, I have noted also, that after cyclodiathermy these small capillaries often shrink, at least temporarily.

Dr. Roberts: Rubeosis iridis is noted in diabetes, in detached retina, and in some necrotic malignant melanomas. However, the differentiation between the ordinary rubeosis

and the type of vascular changes that occur in thrombosis of the central retinal vein is in the nature of the peripheral anterior synechias and in the nature of posterior segment changes which were demonstrated on the slides.

William I. Glass,
Recording Secretary.

February 24, 1956

CASE PRESENTATIONS

CASE 1

DR. VAN LONKHUYZEN: A boy, aged eight years, on whom a diagnosis of incomplete aniridia was made in February, 1953, showed in his right eye a small peripheral defect in the iris and a large defect on the temporal aspect of the left eye. The vision was correctible to 20/40 bilaterally. In July, 1954, it was noted that the tension on the right eye was 48 mm. Hg and on the left eye 55 mm. Hg (Schiøtz). Treatment was begun with pilocarpine and eserine and originally the tension responded and came down to levels of 25 mm. Hg in the right eye and 25 to 30 mm. Hg in the left eye. This year the tension has varied and has been up to 40 mm. Hg in the right eye and 45 mm. Hg in the left eye. Gonioscopy showed that the iris was far forward in the angle with extensive synechias hiding Schwalbe's line. Aqueous outflow studies showed figures of 0.14 on the left eye and 0.07 on the right eye. This was presented as a problem for treatment.

Discussion. DR. LOUISE LOVEKIN: This case is not like the usual congenital glaucoma where the angle is filled with loose tissue, but here the iris comes right off the cornea. In the area of the aniridia, the stub of the iris is reflected right on the cornea. This is more like a picture of narrow-angle glaucoma but with a deep chamber. There is considerable vascularization in the area of the angle. No optic cupping was noted. The child had considerable difficulty with glare and an attempt to treat this with pinhole glasses was unsuccessful.

DR. WIES: Goniotomy in this type of case would probably be hazardous because of the bleeding, which is likely to occur.

DR. GLASS: Since almost any intraocular procedure would cause considerable bleeding here because of the vascularization, would not cyclodiathermy be the operation of choice? A preliminary attempt to find out whether tension is affected by Diamox therapy might help in deciding on cyclodiathermy or any surgical procedure.

DR. LOVEKIN: Two cases of aniridia have been reported with successful results following goniotomy.

DR. GUIDA: It is interesting that the child responds to miotics.

DR. FREEMAN: The blood vessels of the iris are somewhat different from other blood vessels and merely cutting them is not necessarily a threat, because they soon stop bleeding. However, with the fields normal at the present time, I feel perhaps nothing should be done at present, except careful observation for any possible field loss before surgery is attempted.

DR. FASANELLA: Dr. Blake favored cyclodiathermy here. In one case in his experience, this was repeated three times with good results in one eye, whereas in the other eye the vision was lost with hemorrhage from a goniotomy.

DR. VAN LONKHUYZEN: Dr. Chandler, in talking about acute glaucoma, was all for early operation if any tendency for recurrence was noted. In wide-angle glaucoma, the possibility of improvement from operation would be just as favorable at a later date as if it were done early, and in this case it might be well to wait.

DR. WIES: I feel that, since we know so little about glaucoma and especially glaucoma in this particular condition, conservative therapy is the treatment of choice until something changes in this condition, inasmuch as there is no field defect yet. I do not have any objection to the use of Diamox, although, in general, long-term use of Diamox is not too satisfactory.

CASE 2

DR. DESUTO NAGY: A 51-year-old man was first seen in 1945 with a presenting symptom of progressive deterioration of vision, lasting for eight days. The retina showed a typical solid detachment without holes, with no pigment scattering, and with a dark shadow on transillumination. The anterior segment of the eye was entirely clear. The ocular tension was normal and the other eye was normal. At enucleation, there was no evidence of a local extension and there were no evidences of distant metastases on complete physical examination. No pigmented cutaneous nevi were noted.

In June, 1954, nine years later, the patient was operated on at another hospital for acute appendicitis. This was found but, in addition, numerous pigmented masses, consisting of massive metastases of melanoma were found in the omentum and in the mesoappendix. The patient is still alive, 11 and one-half years after enucleation. This case is presented as another one to demonstrate that ocular melanomas may produce delayed metastases, just as cutaneous melanomas are known to do, long after apparently adequate removal of the primary site.

Discussion. DR. FASANELLA: What is the five-year survival rate?

DR. FREEMAN: Recent statistics would be important in this regard but there is a high recurrence rate.

William I. Glass,
Recording Secretary.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

March 15, 1956

DR. I. S. TASSMAN, *Chairman*

KERATOTOMY IN MOOREN'S ULCER

DR. R. D. HARLEY (by invitation): Mooren's ulcer is a relatively rare disease. In the available literature it was unusual for one ophthalmologist to have reported more than three cases of his own even after working for many years.

In over 25 percent of cases it is bilateral but several years may elapse between involvement of each eye. It characteristically occurs in elderly people but case reports include all ages.

The disease begins with a gray patch of infiltration at the corneal margins approximately one mm. from the limbus. The ulcer spreads slowly along the margin and gradually in toward the corneal center. After the ulcer has been present for two weeks or longer a dehiscence or furrow becomes apparent along with an overhanging margin with its base on the corneal side. The ulcer penetrates about one-half way through the cornea and never appears to go deeper. Perforation is rare unless secondary infection is present. Healing takes place very slowly from the periphery with the development of new vessels and scar tissue. In front of the advancing border there is a gray infiltration and beyond this point the cornea remains completely clear.

Symptoms of pain and photophobia are very severe in spite of the mild tissue response to inflammation. The eye pain is not controlled by the use of local anesthetics. In addition to the local eye discomfort, the pain seems to involve most of the area supplied by the first division of the fifth nerve. Even heavy sedation may give but temporary relief and the increasing exhaustion of the patient becomes as much of a problem as the eye. Unfortunately, in too many cases, despite all treatment available, the pain and ulcer continue unabated and the prognosis for future vision becomes poor.

A case involving both eyes was presented which was successfully treated by delimiting keratotomy after a conjunctival flap failed to help. Penetrating keratotomy incisions from the 11- to 7-o'clock positions and 7- to 4-o'clock positions were required for

the left eye but quadrilateral keratotomies were required for the right eye.

Involvement of the second eye took place 18 months following the attack in the first eye. The visual acuity has remained at 20/30 in the right eye and 20/70 in the left eye for the past three years and there has been no sign of recurrence.

The production of hypotony over a period of time seems to offer good results. This can be accomplished by delimiting keratotomy, repeated paracenteses, or making a fistulous track with a cautery. A ring-shaped, lamellar corneal graft has received good reports and may be used prior to a keratotomy.

Discussion. DR. GLEN G. GIBSON: Dr. Harley should be congratulated for his heroic efforts and his gratifying end-result, which he has achieved in a condition that all too frequently terminates in blindness or in enucleation. He was kind enough to permit me to see this patient, and I wish to confirm his diagnosis. His description does not adequately portray the hopeless appearance of these eyes and the intractable nature of Mooren's ulcer of which his patient has a classical example in every detail. He has stated that the basic abnormality and pathogenesis of Mooren's ulcer is unknown. The clinical course, the response to therapy, and the way in which repair was accomplished would tend to suggest that diminished nutritive supply, secondary to vascular sclerosis, played an important role in the pathogenesis of this process. Such a simple explanation does not suffice, however, due to the common occurrence of the advanced stage of vascular sclerosis and the infrequent incidence of Mooren's ulcer. The delimiting keratotomy is admittedly an empirical procedure, and the benefits from this operation can presumably be attributed to two main and different mechanisms. Firstly, the delimiting keratotomy has a confining influence on the necrotic process in corneal disease which at times spreads by the necrotic tissue's necrotizing effect on the adjacent vital cells by direct continuity. A delimiting keratotomy tends to prevent this type of extension, and that is one mechanism by which benefits were probably derived.

The other beneficial effects are related to hypotony. Presumably a number of alterations occur following prolonged hypotony. These alterations are not easy to measure, but it can be postulated that increased secretory activity by the ciliary processes, leading to a plasmoid aqueous, accounts for some of the beneficial effects. Dilatation and migration of vascular loops of superficial limbal plexus occurs. This is essential to repair in this process. Likewise there is a reduction in tissue tension, which has a beneficial effect on the transfer of intracorneal fluid. There is increased permeability of the cornea, due to the obvious discontinuity of the epithelium and endothelium. The keratotomy may accelerate the elimination of the toxic material from the necrotic ulcer.

The use of chemical cautery and diathermy is said to be beneficial in the treatment of this condition, but it should be done with a clear-cut concept of the difference in the therapeutic objective in pyogenic ulcer and in Mooren's ulcer.

In cases of purulent corneal ulcer, diathermic fulguration is the method of choice. It should be the principal method for eradication of the infection, and antibiotics should be reserved for a secondary role in most cases. The objective is not only to destroy the necrotic tissue, but to extend beyond the visual limits of the lesion to destroy the organisms, which presumably are located beyond the visible margins of the lesions. To be successful diathermic fulguration should be done in a somewhat radical manner.

In contrast to this, in Mooren's ulcer the objective is merely to destroy necrotic tissue, and not to eradicate infection. The fulguration with diathermy should be done in a highly conservative manner, because here we are employing a very devitalizing agent in a tissue which is already devitalized. I should like to emphasize a point which Dr.

Harley passed over rather lightly, and that is the fact that part of his success was due to the fact that he closely adhered to one of the basic principles in corneal therapy. He kept the eye thoroughly atropinized. The incomplete or inadequate utilization of atropine constitutes one of the greatest therapeutic errors in present-day ulcer therapy.

Finally, I think that we can all approach our next case of Mooren's ulcer with a sense of diminished futility after hearing Dr. Harley's interesting case report.

Dr. James S. Shipman: I would like to compliment Dr. Harley on his beautiful result. My own experience with this operation in other types of malignant ulcers has been very satisfactory. I do not think this procedure has been done or is being done as much as it should be. We used to refer to this operation, and I still refer to it, as a Saemisch section, and I think I must have done at least four or five, and I have been present when another five or six have been done.

This operation was first called to my attention by Dr. B. F. Baer about 25 years ago. I will never forget the first one I saw him do, how brutal it looked, and how I felt that the patient would never see again. But, gentlemen, it does work, especially when it is done soon enough. I think Dr. Harley is to be congratulated that he had nerve enough to try this procedure in a case of Mooren's ulcer, and to do it as it should be done. Certainly, it proved to be perfect for this case, and it did stop the progress of the condition. I have seen it work in other cases and save eyes that would otherwise have been lost, but not always saving so much vision as he did here.

Electroretinogram during blackout

Dr. T. D. Duane, (by invitation): Electroretinograms from five subjects were recorded on the human centrifuge under varying degrees of accelerative stress up to and including blackout and unconsciousness. These findings were correlated with the changes in the retinal circulation and with the consensual light reflex. It was found that the electroretinogram could not be employed as an objective measurement of blackout since it persisted throughout all the experiments, as did the consensual light reflex. These findings indicate a likely origin of blackout in or near the ganglion-cell layer of the retina.

Discussion. Dr. Francis H. Adler: Dr. Duane, we are all fascinated by your work and the amount of torture that you have put yourself through in this experimentation concerning the possible site of blackout. I cannot see from your diagram how pupillary impulses get through, while visual impulses are blocked, unless you postulate separate optic nerve fibers for these functions.

I wonder if it would be helpful to perform another experiment, and that would be to record under these conditions an electroencephalogram with the ordinary alpha rhythm and see whether you can still get "driving" through. The alpha rhythm can be influenced with intermittent illumination from the retina. In other words, if you expose an eye to flicker, you can under normal conditions show the influence of flicker on the rate of the cortical impulses. That is called driving the alpha rhythm.

Now I would like to know whether under conditions of blackout you can demonstrate "driving." If you cannot, it means impulses are not reaching the cortex, and that would mean that blackout is solely in the retina. If you can still get driving, it would mean that blackout may be partially in the retina and partially in the cortex.

Dr. T. D. Duane: In the first place I would like to thank Dr. Adler for his comments. When you say that you are not quite certain as to our scheme, is that because of a poor diagram or because you do not believe it to be physiologically possible?

Dr. Francis H. Adler: Well, let us assume that the ganglion cell is the last point at which blackout could affect the

retinal conduction unless you are going to assume it is on the nerve fiber. Let us take the ganglion cell. Now, if it is anywhere between the ganglion cell and the receptors why would it not block the pupillomotor fiber as well as the visual?

DR. T. D. DUANE: First, let me state we think that the synapse is more susceptible to anoxia than the ganglion cell itself.

Now there are quite a few synapses in between the photoreceptor and ganglion cells. We have pinpointed to this particular synapse, because we think the other synapse between the photoreceptor and the pupillomotor afferent tract is deeper in the retina, more in the deep bipolar region, or closer to the photoreceptor itself. This receives a certain supply of oxygen, and so forth, from the deeper portion of the retina, also from the choroid. Now the ganglion cell and the ganglion synapses lie within the outer bipolar area. This area does not get anything, or very little, from the deeper source of the supply for the retina—I mean that closer to the photoreceptor cell. So we conclude that when reflex action occurs under these conditions of blackout that photoactive and relatively insensitive nerve fibers continue to function. We think that, in the visual pathway, the photoreceptor and bipolar areas function but that the impulse is blocked at the region of synapse between the ganglion cell and bipolar area where the blood supply has been cut off, as we observed.

Anyway that is the theory. You see it seems there are not the same number of synapses and pathways for pupillary as there are for visual fibers.

DR. FRANCIS H. ADLER: That is the assumption that you accept. In other words, all the evidence points to them being the same.

DR. T. D. DUANE: And that is not what you say in your book.

DR. FRANCIS H. ADLER: The *Bible* says, "Would that mine enemy would write a book." The evidence is certainly not conclusive that they are separate. Many have tried to make them separate because of so many clinical facts which suggest it.

DR. T. D. DUANE: You are right. As I say, the tendency is for the physiologic basis to help support the anatomic. I do not think there is good evidence for either, but the second part of your comment, about the photic driving, is very interesting.

Dr. Lewis and I, before he left, had proposed experiments in which we planned to do this very thing. Both under room conditions that is; pressure on the globe plus during blackout on the centrifuge. However, Dr. Lewis is now measuring intravascular phenomena and so I do not know if we will get to it.

William E. Krewson, 3rd,
Clerk.

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SPRING MEETINGS 1957

The remarkable total of 78 papers was presented to unusually large and interested audiences at the annual meetings of the American Ophthalmological Society, the Section on Ophthalmology of the American Medical Association, and the Association for Research in Ophthalmology. Nearly every paper was followed by an assigned, prepared, and competent discussion so that at the end of the meetings one had been presented with an almost overwhelming mass of data, charts, Kodachromes, triumphs, tragedies, and the other ingredients which make for lively medical gatherings.

The 93rd annual meeting of the American Ophthalmological Society was held at The Homestead, Hot Springs, Virginia, May 30, 31, and June 1, 1957; 135 members and 23 guests attended the three one-half day ses-

sions over which Frederick C. Cordes presided. Nineteen papers of broad interest were presented and, as always, the exchange of ideas and experiences made the discussions which followed unusually interesting.

Robert Shaffer indicated the value of gonioscopy as an operating room procedure in which, following paracentesis, the anterior chamber is deepened with saline in the angle-closure types of glaucoma to learn if the angle is open so that peripheral iridectomy will be effective. If the angle is nearly closed by goniosynechias, Chandler's goniotomy or a cyclodialysis is indicated. C. Wilbur Rucker, basing his historical study on Sir Issac Newton's 15th query appended to "Opticks," which concerns the semidecussation of the optic nerves at the chiasm, presented a charming and delightfully illustrated inquiry into Newton and his times. The meetings were never so long that they became tedious, the weather was fair, the ladies lovely, the golf, tennis, skeet, fishing, riding, and visiting pleasant, and the meeting was most enjoyable.

The Howe Medal was awarded to Georgiana Dvorak-Theobald, a selection which met with enthusiastic and prolonged applause. Henry Wagener, chairman of the Committee on Prizes, presented the medal with a carefully documented and light sentimental résumé of Dr. Georgiana's contributions to teaching, research, pathology, the American Board, and to meetings and discussions.

Walter S. Atkinson of Watertown, New York, was elected president and Derrick Vail of Chicago, Illinois, vice-president for 1958. Maynard C. Wheeler was re-elected secretary-treasurer and Gordon M. Bruce, editor of the *Transactions*. The next meeting of the society will be held at the Greenbrier, White Sulphur Springs, May 29, 30, and 31, 1958.

The Association for Research in Ophthalmology meeting dominated the joint session held in conjunction with the Section on Ophthalmology of the American Medical Association. Even with the heartless exclusion of excellent topics, the final program totaled 40 papers, some highly specialized and of limited interest but others of broad clinical application. Surprisingly, even the sessions dealing with unusually erudite and complex studies were well attended and made it evident that a vigorous, original, and provocative group of investigators is emerging in American ophthalmology; 285 registered for the sessions.

The first Friedenwald Memorial Lecture was given by Dr. John E. Harris of the University of Oregon, who spoke on the "Physiologic control of corneal hydration." The Proctor Medal recipient was Dr. Norman Ashton of England who spoke on "Ocular vascularization in health and disease." The studies on retrolental fibroplasia in time may indicate the cause of diabetic retinopathy and studies concerning the role of hypoxia in neovascularization are being directed in that direction. At the annual banquet, Ashton's remarks concerning the honor of being the Proctor Medal recipient: preparation of a biography, a bibliography, a photograph, a light talk for the banquet, and an erudite lecture for the scientific session, and an unforgettable discussion of the preparation of a paper on hepatectomy set a serio-comic standard for years to come.

It was obvious that the Association for Research program is rapidly outgrowing the joint meeting with the section and plans were presented for an interim meeting in January so as to reduce the large number of papers at the June meeting.

Theodore E. Sanders of Saint Louis, Missouri, chairman of the Association for Research, arranged an extraordinary interesting meeting which, despite the number of papers read, adhered to the time schedule most exactly. He will be succeeded by Michael J. Hogan of San Francisco, California. Alson E. Braley of Iowa City, Iowa, was elected a new trustee and Lorand V. Johnson of Cleveland, Ohio, was re-elected secretary-treasurer.

The Section on Ophthalmology of the

American Medical Association sessions, under the leadership of the chairman, Algernon B. Reese, were outstanding. Prof. Jules François of Ghent, an invited foreign guest, spoke on the "Differential diagnosis of tapetoretinal degeneration" in an extraordinarily competent and comprehensive manner. Frank W. Law, of London, spoke on "Iridencleisis in buphthalmos" with that lightness, erudition, and excellence which seems to characterize all ophthalmic visitors from the British Isles.

The business meeting of the section was much more routine than has been customary during the past decade, due largely to the interpretation of the Constitution and By-Laws of the American Medical Association that the purpose of the various sections is to present forums on the scientific aspects of medical practice. All other aspects, social, political, and economic, are within the purview of the House of Delegates of the association. However, thanks largely to the vigorous representation by Harold G. Scheie, secretary of the section, and other officers, the section will be permitted to carry on liaison activities with committees of other national ophthalmic groups. The oral report of the representative to the American Board of Ophthalmology acknowledged the many valuable expressions of opinion received concerning the establishment of a Board of Ophthalmic Surgery and announced that plans for establishment of such a board have been discontinued.

A group of 14 ophthalmic exhibits was presented. The section prize of $250.00 was presented to David Volk, Western Reserve University School of Medicine, for the exhibit, "Conoid ophthalmic lenses: An original development in subnormal vision aids." This exhibit received a certificate of merit, as did the exhibit "Cancerous and precancerous melanosis of the conjunctiva" by Algernon B. Reese and Bradley R. Straatsma of the Institute of Ophthalmology of Presbyterian Hospital and Columbia University College of Physicians and Surgeons, New York. Visual acuity, Harrington visual field screening, and intraocular pressure were recorded in over 500 physicians by the National Society for the Prevention of Blindness in an exhibit directed toward annual physical examinations sponsored by the American Academy of General Practice. The section prize of $250.00 for the best paper presented at this meeting was awarded to Dr. James E. Bennett and Dr. Arby L. Bailey of Cleveland, Ohio, for their paper, "A surgical approach to total xerophthalmia through transplantation of the parotid duct."

The Gold Medal of the section for service in ophthalmology was awarded to Dr. William L. Benedict of Rochester, Minnesota, who has participated in almost every phase of ophthalmology and contributed enormously of his energy and talents to education, administration, and leadership in ophthalmology. Officers of the section for 1958, are: Chairman, Dohrmann K. Pischel, San Francisco, to succeed Algernon B. Reese; vice-chairman, Ralph W. Danielson, Denver, to succeed Hedwig Kuhn. Harold G. Scheie continues as secretary and Ralph O. Rychener as delegate to the House of Delegates with Harvey Thorpe as alternate. Frank W. Newell continues as the section representative to the Committee on Scientific Exhibits.

The Herman Knapp Medal, which was awarded in 1953 to Charles K. W. Ascher for his paper on "Aqueous veins," and prior to that, in 1939, to Frederick C. Davis for his paper on "Primary tumors of the optic nerve," was awarded to Goodwin M. Breinin of the New York University Postgraduate School of Medicine for his paper read in 1955, "The nature of vergence revealed by electromyography." Dr. Breinin has opened a new method of approach to the nature of ocular muscle innervation, developed a valuable method of diagnosis, and well deserved the recognition for his contribution to fundamental and clinical research.

The final day of the meeting was featured by an unusually interesting series of papers on cataract extraction. The operation con-

tinues to excite the same interest in the ophthalmologist that "Hamlet" does in the actor and the session was unusually well attended.

The next meeting of the Section on Ophthalmology and the Association for Research will be in San Francisco in June, 1958.

Frank W. Newell.

INTERNATIONAL COUNCIL OF OPHTHALMOLOGY

The annual meeting of the International Council of Ophthalmology was held in London at the Royal College of Surgeons on April 10, 1957.

There were present: Duke-Elder, president; Berens, vice-president; Hartmann, secretary; Amsler, treasurer; Alvaro, Brazil; Arruga, Spain; Bietti, Italy; Charamis, Greece; Coppez, Belgium; Franceschetti, Switzerland; Lyle, Great Britain; Marshall, Canada; Palomino Dena, Mexico; Paufique, France; Samuels, United States of America; Thiel, Germany; Weve, Holland.

There were also present: Copper, co-opted secretary in charge of the *Index Ophthalmologicus*, and François, the secretary-general of the XVIII Congress.

A résumé of the main business of the meeting is as follows:

Regrets were expressed for the death of Sir Jamshedji Duggan who represented Asia on the International Council; and congratulations were sent to Professor Márquez in Mexico, the president of the XIV International Congress in Madrid in 1933, on the attainment of his 85th birthday.

The treasurer's report showed that the finances of the council were in a healthy condition, most countries internationally federated having paid their dues. It was reported that the Department of Health at Washington had given a grant of 10,000 dollars toward the organizational expenses of the XVIII Congress in Brussels and to aid in the publication of the *Proceedings*. This gift was warmly welcomed.

The Gonin Medal for 1958 was awarded to Prof. Alan C. Woods of Baltimore.

The statutes of the International Federation, of the International Council, and the rules for running international congresses were considered in detail. It may be recalled that these were provisionally adopted at the International Congress in 1954; the revised rules will be supplied to all delegates of the federated ophthalmologic societies throughout the world, and it is hoped that these rules will be finally adopted in the Congress at Brussels next year.

The report of the Committee for the Testing of Color Vision in Transport Workers was passed unanimously. Pseudoisochromatic plates are recommended as a means of testing, either those of Ishihara or the Swedish test of Boström of 1950. This will be brought up to the meeting of the Federation in 1958 for confirmation.

The Polyglot Dictionary of Ophthalmological Terms was discussed. This publication is now at a far-advanced stage of preparation and it is hoped that it will be available for sale at the Congress in Brussels. The dictionary is in five languages—English, French, German, Latin, and Spanish.

The affiliation of supranational societies (groupings of regionally related nations) with the International Council was considered. It will be remembered that the Pan-American Association of Ophthalmology is associated with the council in this way and sends a representative to its meetings. The progress of the development of a corresponding Pan-European Society of Ophthalmology was considered, and the council decided to await its further development during the next year in the hope that the federation would agree to its affiliation also. There is a similar movement to form an Asia-Pacific Academy of Ophthalmology representing nations bordering the Pacific Ocean; the council also hopes that the organization of this new body would have advanced sufficiently to give consideration to it in 1958.

A request for the admission of the Polish

and Rumanian Ophthalmological Societies to the federation was received from these countries; to this the council agreed on completion of the necessary formalities.

A report of a subcommittee to decide on the methods of inviting delegates to international congresses was received and agreed. In essence it was decided that invitations could be made through diplomatic channels or, alternatively, the consent of the government of the host country having been obtained, through ophthalmologic channels, whichever method was easier in any particular case.

A suggestion that clinical research should be correlated in different countries throughout the world by the International Council was discussed but a decision on the subject was postponed until the next meeting of the council.

The president (Coppez) and the secretary-general (François) of the XVIII International Congress to be held in Brussels in September, 1958, reported on the progress of their arrangements. It would appear that both from the scientific and social points of view the meeting promises in every way to be a success.

The centenary of international ophthalmology. In view of the fact that the first International Congress was held in 1856, the president was charged in 1956 to write a short history of the first hundred years of international ophthalmologic relationships. The proofs of this book were laid on the table and it was decided that the council should present it as a gift to delegates attending the International Congress in 1958; thereafter the book will be sold on the open market.

A report was received from Copper on the state of the publication of the *Index Ophthalmologicus* for 1958. Preparations of this volume are well in hand and it will comprise some 350 pages. Arrangements have been made for it also to be distributed to all delegates to the International Congress. It was also noted that there were some 1,000 copies of the *Index Ophthalmologicus* published in 1954 as yet unsold; in view of the fact that a new edition will appear in 1958 it was decided that a copy of the old *Index* would be sent free of charge to any ophthalmologist who applied for it.

The President of the Professional Association of German Ophthalmologists appealed to the council to put on record their opinion initially given in 1933 that refraction of the eye was essentially a medical act which should be performed by medically qualified people; this the council confirmed.

It was noted that the German Ophthalmological Society would celebrate its 100th anniversary in September, 1957. All members of the council were cordially invited by Thiel to take part in this meeting.

The next meeting of the International Council was fixed to take place in Brussels on September 6, 1958.

Stewart Duke-Elder.

OBITUARIES

ARTHUR M. YUDKIN
(1892-1957)

Dr. Arthur M. Yudkin, clinical professor of ophthalmology at the Yale Medical School, died of a heart attack May 2, 1957, while driving to his home in Woodbridge, Connecticut. He was buried on May 5, 1957, following memorial services in the Congregation Mishkan Israel.

Dr. Yudkin is survived by his wife, the former Adele I. Weissman of Woodbridge, whom he married in 1920, and two sons, Marvin Yudkin and Dr. Gerald Yudkin of St. Paul, Minnesota. There are also three grandchildren.

Dr. Yudkin was born in Ansonia, December 31, 1892, the son of Michael and Minnie Zandler Yudkin. He received his Ph.B. degree from the Yale Sheffield Scientific School in 1914 and his M.D. degree in 1917, also from Yale.

He was assistant resident physician at New Haven Hospital from 1917 to 1918 and

an intern in ophthalmology in 1918. From that year to 1921 he was clinical assistant in ophthalmology and laryngology in the Yale School of Medicine and for the next four years was clinical instructor in ophthalmology.

His promotions at the School of Medicine began in 1925 when he was made assistant clinical professor; in 1928, he became associate clinical professor, and in 1934 was promoted to a clinical professor of ophthalmology.

In addition to his large private practice, Dr. Yudkin was attending surgeon in ophthalmology at Grace-New Haven Hospital, attending ophthalmologist at the Hospital of St. Raphael, and consulting ophthalmologist at Griffin Hospital, Derby, Bristol Hospital and to the National Society for the Prevention of Blindness.

In 1943, Dr. Yudkin was commissioned a major in the Medical Reserve Corps. He was a member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, National Society for the Prevention of Blindness, Society for Experimental Biology and Medicine, New York Academy of Medicine, Society of Clinical Ophthalmology, Sigma Xi honorary society, Milford Yacht Club, Race Brook Country Club, and Yale Faculty Club.

Dr. Yudkin was co-editor of the *Practitioners' Library of Medicine and Surgery*. He contributed more than 54 scientific articles pertaining to ophthalmology. His chief interests were vitamin-deficiency diseases and vitamin therapy. He wrote many fundamental articles on these subjects of value to ophthalmologists.

R. M. Fasanella.

HARRY VINCENT JUDGE
(1889-1957)

Harry Vincent Judge was born in Albany, New York, on May 11, 1889, and died in Albany Hospital on March 3, 1957, of cerebral thrombosis. The son of Patrick Henry Judge and Susan E. Mullen, both of Albany, he was married on December 22, 1922, to Cornelia Mills, the daughter of Arthur D. Mills and Cornelia Knower, who survives him, as does his only son, Dr. Harry Mills Judge, and three grandchildren.

After graduating from Albany Medical College in 1914, Dr. Judge had a general internship of one year in Albany Hospital and then a residency in ophthalmology at Wills Hospital in Philadelphia. World War I took him overseas where he served in several base hospitals with the rank of captain. On his return to Albany in 1919, he received appointments on the staff of the Albany Medical College and Albany Hospital, serving both institutions for 35 years. From 1927 until 1954, he was head of the Department of Ophthalmology, and upon retiring was named emeritus professor. He also served as attending and consulting ophthalmologist on the staffs of the Anthony M. Brady Maternity Home, St. Margaret's House and Hospital, and the Greene County Memorial Hospital.

Dr. Judge was a member of the Alpha Omega Alpha honorary medical fraternity. He received the diploma of the American Board of Ophthalmology in 1921. Besides belonging to his county and state societies and the American Medical Association he was a fellow of the New York Academy of Medicine, a member of the American Academy of Ophthalmology and Otolaryngology, a charter member of the Eastern New York Eye, Ear, Nose, and Throat Association, and a member of the Wills Hospital Alumni Association. He was one of the very few members from outside the metropolitan area to be elected to the New York Ophthalmological Society, an honor which he treasured highly and, until ill health intervened, he rarely missed a meeting.

Although not a voluminous contributor to the literature, Dr. Judge had a special interest in the eye problems of children and published papers on "The value of early

probing for tearing and infections" and on "Ankyloblepharon filiforme adnatum."

His social clubs included the Fort Orange Club, the Albany Country Club, and the University Club.

No bare recital of vital statistics can give any clue to the personality that was Harry Judge. One would have to observe him enter a restaurant in the city where he spent his entire 67 years, to the accompaniment of "Hi, Harry," "Hello, professor," "Good afternoon, Dr. Judge," as he progressed to his seat, to realize the affection in which he was held. Or to see him stop his car along a country stream, get out and clamber down the bank to inquire with genuine interest of a totally strange fisherman (a "brother of the angle" was his expression) how they were biting. At a social gathering no one told a story better, or listened more appreciatively. He was an ardent photographer, particularly during his vacations at Edgartown on Martha's Vineyard and in Europe, but his friends were never bored with unsolicited exhibitions of his pictures. And in the spring and fall he liked to get off occasionally with some of his cronies for a convivial weekend without ophthalmologic shop talk. This was the Harry Judge whose friends were legion; sorely will they miss him.

W. Guernsey Frey.

CORRESPONDENCE

Viability of frozen corneas

Editor,

American Journal of Ophthalmology:

We have read with interest the paper "Viability of corneal epithelium and fibroblasts after long-term storage" by Cockeram. Basu, and Ormsby in the March (1957) issue of The Journal.

We would like to point out that although the authors state in their summary: "Corneas frozen by the quick method of freezing and stored at −79°C. in 15-percent glycerin and saline were not viable after one and one-half hours of storage", they appear to have frozen whole eyes.

If protection from the harmful effects of freezing are dependent upon thorough impregnation of the cornea with glycerin, one might expect less protection in the case of whole eyes where the endothelial surfaces are not exposed to glycerin than with excised corneas where the penetration of glycerin should be more complete.

Further in the freezing of whole eyes, even by the so-called "quick method," it is likely that freezing is relatively slow as compared with similar freezing of excised corneas.

In any event, it should be pointed out that this does not seem to be a test of the viability of corneas frozen by the technique originally described by Eastcott (Lancet, Jan. 30, 1954, pp. 237-239).

(Signed) Samuel D. McPherson, Jr.
Jerry W. Draheim
Durham, North Carolina.

Editor,

American Journal of Ophthalmology:

We are indebted to Dr. McPherson and Dr. Draheim for their letter. There has long existed a controversy over the optimal rate of freezing of tissues, and it has been shown in the case of spermatozoa, that slow freezing is best (Polge C., Lovelock, J. E.: Preservation of bull semen at −79°C. Vet. Record, **64**:396-397, 1952).

Smith (Smith, A.U.: Effects of low temperature on living cells and tissues: Biological application of freezing and drying. New York, Academic Press, Inc., 1951, p. 4) stated that "differences of outlook have similarly led to confusion over rates of cooling."

In our experiments, no attempt was made to follow the method of Eastcott, and our "quicker" and "slower" methods were comparative (Am. J. Ophth., p. 382, line 7). "Method A" was quicker than "Method B"

but was not claimed to be identical to the "rapid method" of Smith's classification. In these experiments the slower method was the better method.

We have carried on parallel experiments with excised corneas and have found the results the same, whether the tissue was a whole eyeball or an isolated cornea, using tissue culture methods following Method B.

(Signed) A. Cockeram, P. K. Basu,
and H. L. Ormsby,
Toronto, Ontario.

BOOK REVIEWS

DOCUMENTA OPHTHALMOLOGICA: Advances in Ophthalmology. Jean Nordmann, secretary of the Board of Editors. 'S-Gravenhage, The Netherlands, Dr. W. Junk, 1956. Volume X, 380 pages. Price: 92 Dutch guilders.

This is the 10th volume of this well-known and valuable annual of ophthalmology. As is customary, one finds here papers of great scientific value. The present volume chiefly concerns papers presented at the dedication of the new Bonn University Eye Clinic. These are in German with summaries in French, Italian, and English.

H. K. Müller discusses the planning and building of the new eye clinic; G. Meyer-Schwickerath, his exciting work with light coagulation of the retina and iris; O. Kleifeld, studies on the intracapsular mechanism of accommodation, which is most ingenious.

W. Leydhecker, who is well known for his studies on glaucoma, especially the provocative tests, contributes a paper on the problems in diagnosis and therapy of glaucoma. W. Best and K. Bohnent discuss their studies on dark adaptation and electroretinograms.

There is a report of a round-table discussion of the measurements of the retinal arterial blood pressure held in Bonn on March 9, 1955. Those who took part in the symposium were: von Bahr, Bailliart, M. Baurmann, H. Goldmann, H. Harms, A. Lobstein, H. Miller, J. Nordmann, P. Niesel, R. Pigassou, and E. Weigelin. This will repay careful study for it is a most controversial subject.

N. M. J. Schweitzer's paper is on "The threshold measurements of the light reflex of the pupil in the dark-adapted eye" (in English). This is a monograph of 79 pages with many diagrams and is highly scientific.

The volume ends with an exciting case report by V. Čavka of Besgrad of an apparently successful transplant of a lens from a cadaver. "Subsequent examination of the patient," says the author, "six months after operation, showed the transplanted lens to be still perfectly clear."

Derrick Vail.

CONNECTIVE TISSUE IN HEALTH AND DISEASE. Edited by G. Asboe-Hansen, M.D. Copenhagen, Ejnar Munksgaard; New York, Philosophical Library. 321 Pages. Price: $15.00.

"It is sufficient to know, that all the parts of the Body are made up of Threads or Fibres, of which there be different Kinds; for there are some soft, flexible, and a little elastick; and these are either hollow, like small Pipes, or spongeous, and full of little Cells, as the nervous and fleshy Fibers; others there are more solid and flexible, but with a strong Elasticity or Spring, as the membraneous and cartilaginous Fibers; and a third Sort are hard and inflexible, as the Fibres of the Bones. Now of all these, some are very sensible, and others are destitute of all Sense; some so very small as not to be easily perceived; and others, on the contrary, so big as to be plainly seen. And most of them, when examined with a Microscope, appear to be composed of still smaller Fibres.

"Now these Fibres do first constitute the Substance of the Bones, Cartilages, ligaments, Membranes, Nerves, Veins, Arteries and Muscles. And again, by the various Texture, and different Combination of some or

all of these Parts, the more compound Organs are framed; such as the Lungs, Stomach, Liver, Legs and Arms, the Sum of all which make up the Body." (James Keill, *The Anatomy of the Human Body* [abridged], 1698.)

The importance of the connective tissue in the economy of the body need not be stressed to ophthalmologists who have become accustomed to the addition of hyaluronidase to anesthetics for infiltration and whose patients have been unusually benefited by the use of cortisone in ocular disease. Additionally the origin of the vitreous from the mesenchyme, the histologic structure of the trabecula, and the orbital changes in exophthalmic thyrotoxicosis suggest that the further clinical contributions to ophthalmology from basic research concerning the connective tissue may be anticipated.

This book is composed of the contributions of 23 prominent investigators of the connective tissue. The initial chapters deal with the morphology, morphogenesis, histochemistry, chemistry, and metabolism of the special cells, special protein fibers, and intercellular substance which combine to constitute connective tissue. The spreading reaction and its inhibition are discussed in two chapters. The hormonal reactions, aging, wound healing, and general pathology of the connective tissue are all richly documented. The final chapters discuss the role of connective tissue in infection, cancer, arteriosclerosis, collagen diseases, arthritis, dermatology, and ophthalmology.

In the chapter on ophthalmology, Godtfredsen of Copenhagen discusses the relationship of ocular disease to involvement of the joints (Reiter's disease, rheumatic fever, arthritis), diseases of the skin and mucous membranes (sarcoidosis, dermatomyositis, disseminated lupus erythematosis, and so forth), and blood vessels (periarteritis nodosa and temporal arteritis). This section is essentially clinical with emphasis upon the ophthalmologist participating in the management of mesenchymal disease because the ocular signs may permit initial diagnosis or because of the importance of ocular complications.

This book is hardly one which the clinical ophthalmologist will find of practical value. Nonetheless, one is impressed with the sense of expectancy in the reports, with major advances which appear to be just over the horizon awaiting discovery. The bibliography, the correlation of many scattered reports, and the questions raised make the book of unusual value to the investigator and of considerable interest to the casual reader.

Frank W. Newell.

THE YEAR BOOK OF THE EYE, EAR, NOSE, AND THROAT (1956-1957). Edited by Derrick Vail, M.D., and John R. Lindsay, M.D. Chicago, The Year Book Publishers, 1957. 448 pages, 128 figures, author and subject indices. Price: $7.00.

In this, as in previous volumes, Vail maintains his consistently high standard in the selection and condensation of articles and in the expression of his reactions. As of next year the publication will cease its dichotomy and will be replaced by *The Year Book of Ophthalmology* and *The Year Book of Ear, Nose, and Throat*. This division will result in two full-size volumes, each serving with much greater adequacy the interests of its readers.

With the vastly increased space at Vail's disposal, an editorial preface emphasizing the highlights of the year might be introduced. The dozen years since World War II have yielded the antihistamines, corticosteroids, broad-spectrum antibiotics, hyaluronidase, Isoniazid, Daraprim, Diamox, disodium versenate (EDTA), tonography, and the prophylaxis of the retinopathy of prematurity. Even more dynamic progress may be anticipated in the near future. Among the 1956 contributions is the amazing apparatus of Meyer-Schwickerath's by which precise photocoagulation of a fundus lesion can be guided by direct ophthalmoscopy. The treat-

ment of a flat detachment, angiomatosis retinae, or retinal periphlebitis can become thereby an office procedure just as the cautery of Little's area by the rhinologist for epistaxis. An equally exciting advance is Shafer's use of vitreous implant in detachment of the retina.

Unless an ophthalmologist is familiar with the literature rare conditions such as Oguchi's disease, Werner's syndrome, or Wegener's granulomatosis could hardly be recognized when encountered. But the better ways of handling usual cases should not be neglected. Only two minor articles relating to refraction are presented and none on current developments in optical aids for subnormal vision. The reader who is seeking guidance would undoubtedly appreciate more extensive editorial comment. Accompanying each *Year Book* is a questionnaire designed to test familiarity with current literature. This can be a valuable means of focusing attention to the essentials and more care in its preparation would be very worth while.

The present volume is excellent—but next year's should be worth waiting for!

James E. Lebensohn.

CURRENT THERAPY: 1957. Edited by Howard F. Conn, M.D. Philadelphia, W. B. Saunders Company, 1957. 690 pages and index. Price: Not listed.

This annual publication contains, as usual, very little of ophthalmologic interest. There is included, however, a most complete list of the poisons found in various household items and commercial preparations and a helpful chapter dealing with the treatment of various forms of poisoning. There is a rather complete roster of drugs, listed by proprietary rather than pharmacopeial names, and a list of laboratory values of clinical importance.

William A. Mann.

OPTICS: THE SCIENCE OF VISION. By Vasco Ronchi, Ph.D. Translated from the Italian by Edward Rosen. New York, New York University Press, 1957. 360 pages, 128 figures, index. Price: $10.00.

Ronchi, a physicist and director of the National Institute of Optics in Italy, invented the Ronchi optical test in 1923 which has achieved world-wide acceptance. The present book, translated by a historian, is written in narrative style with no bibliography, a minimum of mathematics, and illustrated with the simplest figures. It is not a textbook, but rather a polemic tract for what he terms energy optics and emphasizes the interplay of physical, physiologic and psychologic factors in anthropomorphic optics. He notes that in the face of disagreement between optical reports and information derived from memory and environment the mind usually prefers the latter. When a convex lens is held within its focal length over a printed page, the image should be farther away than the paper, but the magnified image is seen in the plane of the paper. The optical image and the subjective image are not the same. Lenses showing defects intolerable to observers with acute sight may be satisfactory for observers with inferior acuity. In vision, as in photography, the outcome depends on the radiant energy emitted by the source, the distributing system, and the detecting layer. The retinal image reflects the distribution of energy effects on a photosensitive membrane. From a so-called point stimulus the brain receives impulses from cones affected by the central stimulus and from surrounding cones. The effigy created comes to have accordingly the form of a star. The smallest angle resolvable by the naked eye is a function of the logarithm of the intensity of the source with a central maximum at optimum intensity and descending slopes for both increasing and decreasing intensities.

The book is stimulating, especially in the brilliant historical review of optical progress, but the author's excessive concern with the derogation of geometric optics results in a confusing exposition.

James E. Lebensohn.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

1

ANATOMY, EMBRYOLOGY, AND COMPARATIVE OPHTHALMOLOGY

Niessen, V. **The morphology of the lens epithelium.** Ophthalmologica **132**:125-128, Aug., 1956.

In 1951 François and Rabaey reported on examinations of fresh unstained lenses with the phase-contrast microscope (Brit. J. Ophth. **35**:352, 1951). In addition to the typical well-known polyhedral epithelial cells the Belgian authors found another type which they described as dark, star-shaped, with protoplasmic prolongations which extend between the polyhedral cells. Restudy of the matter by Niessen, also with the phase-contrast microscope, has failed to reveal that second type of cell. The discrepancy in the findings may be due to artifacts. (2 figures, 4 references) Peter C. Kronfeld.

Pau, Hans. **Cell division in the corneal stroma.** Ophthalmologica **132**:230-235, Oct., 1956.

Cytologic study of the process of wound repair in the corneal stroma (of the rabbit) reveals that the earliest cells appearing near the scene of the trauma are the product of local, that is stromal, cell division. (7 figures, 7 references)

Peter C. Kronfeld.

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Damiani, Alessio. **Re-epithelialization of the cornea after subconjunctival antireticulous histiocytes.** Rassegna ital. d'ottal. **25**:281-287, July-Aug., 1956.

The author studied experimentally the action of a cytotoxic antireticuloendothelial serum, injected subconjunctivally, to determine the reparative power of the surface of the cornea. In the eyes treated there was complete repair of the epithelial loss in a time two thirds of that required in the untreated control. (29 references)

Eugene M. Blake.

Morawiecki, J. **Precipitation phenomena due to antigen-antibody reactions in the living cornea.** Ophthalmologica **132**: 236-243, Oct., 1956.

A parallel is drawn between precipitation phenomena that occur in sheets of agar in which depots of an antigen and its antibody have been made several centimeters apart, and opaque streaks developing in the corneas of experimental animals which have been inoculated with antigen and antibodies several millimeters apart. In the latter case opaque streaks make their first appearance about 24 hours after and half way between the sites of the in-

tracorneal inoculations, increase in density for several days and disappear in about two weeks. Histologically the streaks are made up of leucocytic infiltrations. Intracorneal injection of antigen only, such as the serum protein of a different species, elicits crescentic or ring-shaped corneal infiltrations which slowly migrate from the periphery toward the center of the cornea (the phenomenon first systematically studied by Wessely). This phenomenon may be due to the diffusion into the cornea of antibodies produced by the host. General diseases such as annular keratitis may be due to a mechanism of this sort. (5 figures, 8 references)

Peter C. Kronfeld.

Rempt, F. **Clinical significance of the Shwartzman phenomenon.** Ophthalmologica **132**:133-136, Sept., 1956.

Raus, R. **The induction of the Shwartzman phenomenon in the rabbit cornea.** Ophthalmologica **132**:137-140, Sept., 1956.

In the first article Rempt gives a general description of the Shwartzman phenomenon, that is of the localized necrosis with hemorrhage which occurs at the site of an intracutaneous injection of a sterile bacterial filtrate if the same or a similar bacterial filtrate is injected intravenously 24 hours later. There exist now a good many modifications of the Shwartzman phenomenon. The fundamental local tissue change seems to be due to a lowered capillary resistance. Shwartzman phenomena may be the basis of vitreous hemorrhages occurring in the course of tuberculin therapy of retinal perivasculitis. By a similar mechanism vitreous hemorrhages may be brought on in cases of intestinal infestation with ascaris lumbricoides.

In the second paper Raus describes a Shwartzman phenomenon in the rabbit cornea. It was produced by 1. injecting alloxan into the anterior chamber which caused partial vascularization of the cornea, 2. injecting a filtered broth culture of typhoid bacilli into an avascular portion of the same cornea, and 3. injection of 1 ml. of the same filtered broth culture intravenously. Four hours later hemorrhages appear in the vascularized portion of the cornea which at the same time becomes more edematous. Histologically the outstanding features are multiple thromboses and stromal necrosis followed by heavy polynuclear infiltration. Future studies will concern themselves with pharmacologic and, specifically, hormonal effects upon the Shwartzman, phenomenon in the rabbit cornea. (4 figures, 10 references) Peter C. Kronfeld.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Bonavolonta, Giuseppe. **Experimental research on the action mechanism of acetazoleamide (alkali reserve, pH and sodium and potassium level in the aqueous after Diamox treatment).** Arch. di ottal. **60**:219-239, July-Aug., 1956.

After intravenous administration of Diamox to rabbits it was found that in the aqueous the alkali reserve was diminished, the pH slightly raised, potassium reduced and sodium unchanged. These findings confirm the hypothesis that Diamox causes a reduction of the aqueous production. (4 tables, 30 references)

John J. Stern.

Damiani, Alessio. **The fluid uptake of the lens after repeated keratocentesis.** Arch. di ottal. **60**:249-256, Sept.-Oct., 1956.

The fluid uptake of the lens in rabbit eyes after repeated keratocentesis was found to be diminished. (2 figures, 1 table, 16 references) John J. Stern.

Damiani, Alessio. **Modification of the hemato-ophthalmic barrier by the use of anticoagulants and mercurial diuretics.**

Rassegna ital. d'ottal. **25**:186-192, May-June, 1956.

Experimental study of the action upon the hemato-ophthalmic barrier by the administration of anticoagulant drugs, of mercurial diuretics, and of the two combined led to certain conclusions. The blood-ophthalmic barrier was decidedly augmented by the anticoagulants but scarcely influenced by the combined anticoagulant and mercurial treatment. It is known that the anticoagulants act upon the thromboembolic process favorably by anticipating the extension of the obstruction and by dissolving the coagulated blood in the lumen of the vessel. (3 figures, 9 references) Eugene M. Blake.

François, J. and Rabaey, M. **Studies on outflow of aqueous humor.** Tr. Ophth. Soc. Australia **16**:51, 1956.

The rate of perfusion of enucleated eyes is greatly influenced by temperature. Corrected results are necessary for comparison with tonography (1.3 for 20°C.). Hyaluronidase decreases average resistance to outflow by 40 to 50 percent in rabbit eyes but only 25 to 30 percent in human eyes. Resistance remains unaltered because of alterations of pressure from 20 to 80 mm. Hg. The rate of flow is greatly influenced by the depth of the anterior chamber. Increased depth decreases resistance so that results should always be recorded as a function of anterior chamber depth. The regulating mechanism must be located at the level of the iridocorneal angle. Expansion of the scleral trabeculum occurs in deepening the anterior chamber but in narrow anterior chambers the lamellae are folded close together in a fan-like pattern. Increase in pressure in shallow anterior chambers results in more or less complete block of the outflow of fluid. Anatomic changes in the drainage angle cause profound effects upon perfusion outflow. A glaucoma simplex eye had a high resistance (18) and there were unmistakable lesions of the scleral trabeculum, namely, degeneration and thickening of lamellae resulting in obstruction or constriction of the openings. Ronald Lowe.

Heer, Giuseppe. **The blood-aqueous barrier and the electrolytes.** Rassegna ital. d'ottal. **25**:310-318, July-Aug., 1956.

The various theories of the origin of the aqueous humor and the passage of the electrolytes are reviewed. The writer holds that since the ciliary body has a more differentiated structure than the simple walls of the capillaries it is logical to attribute to this structure a greater activity and selectivity. He feels that the ciliary body has the power to excite a quantitative selectivity of the electrolytes from the blood to the aqueous, while the epithelium of the anterior surface of the iris permits a passage of electrolytes from blood to aqueous by simple diffusion. (2 tables, 43 references)

Eugene M. Blake.

Rizzo, P. **Ergographic studies of the effect of digitalis derivatives on the accommodation of asthenopes.** Boll. d'ocul. **35**:543-552, Aug., 1956.

By means of ergography the author investigated the behavior of accommodation in asthenopic patients in whom a digitalis collyrium had been applied. The author's studies indicated a decrease in the fatigability of accommodation upon the local application of digitalis collyrium. (4 figures, 19 references)

William C. Caccamise.

Schweitzer, N. M. J. and Bouman, M. A. **Threshold measurements for the direct light reflex of the pupil.** Ophthalmologica **132**:286-288, Nov., 1956.

The special pupilloscope designed by the authors consisted of 1. a stimulus source variable with regard to area, intensity and wave length, 2. an infrared

light source to illuminate the iris of the eye examined, and 3. an infrared image converter to make the contractions of the pupil visible.

Rhythmic stimuli (flashes) were used in series of twenty and the number of barely perceptible pupillary contractions noted. A 50 percent response, that is 10 contractions in response to 20 flashes, proved to be a threshold of practical value. Such thresholds were determined covering a wide range of variables concerning the stimulus as well as the state of adaptation and retinal area in the eye of the examinee. Many interesting findings were obtained which will be published in detail in the Documenta Ophthalmologica. Most interesting, perhaps, was the finding that the rods act as pupillomotor receptors in the dark-adapted eye. Peter C. Kronfeld.

Stepanik, J. **Postural variations of the pressure in the episcleral veins.** Ophthalmologica **132**:98-105, Aug., 1956.

This study was instigated by Scharf's report before the German Ophthalmological Society (1950 and 1951) that the ocular tension as measured with the Schiøtz tonometer changes significantly as the result of postural changes. During the first 5 to 10 minutes of standing up after the usual tonometry in supine position there is a drop in tension of several millimeters. If the examinee remains standing the ocular tension gradually rises to the reading obtained in the lying-down position. These fluctuations are more pronounced in glaucomatous than in normal eyes. In the paper under review Stepanik reports on measurements of the pressure in episcleral veins in standing-up and lying-down position. The measurements were taken by applying a transparent air-filled pressure chamber to the point of emergence from the sclera (usually a well-formed emissary) of large episcleral veins of the Heerfordt type. Taken in this manner the venous pressure, that is the external pressure which makes the vein collapse, is usually 8 to 10 mm. Hg higher than in an aqueous vein. The author is well aware of the possibility of his method of measurement altering the venous pressure. In the study under review he reports drops, that is relative changes, in episcleral venous pressure occurring as the result of standing up. (2 figures, 2 tables, 9 references)

Peter C. Kronfeld.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Bagolini, B. **A contribution to the recognition of the accommodative effort syndrome of Hill.** Boll. d'ocul. **35**:553-559, Aug., 1956.

The accommodative effort syndrome of Hill consists of asthenopia, blurring of vision during close work, and exophoria for near. Causative factors are an accommodative effort secondary to hyperopia—even of a slight degree—prolonged close work, and incipient presbyopia. Examination of the patient with prisms, base in, and plus lenses will help to differentiate this syndrome from convergence insufficiency. In the accommodative effort syndrome, accommodation and convergence are more readily dissociated by prisms, base in. In such patients the plus lenses will correct the increased dissociability. The author summarizes his findings in three patients who presented this syndrome. (4 references)

William C. Caccamise.

Colenbrander, M. C. **Normal and abnormal localization.** Ophthalmologica **132**:173-176, Sept., 1956.

The author describes and analyzes a number of observations, made by himself with the help of the Maddox wing instrument, pertaining to situations in which visual and haptic localizational clues con-

flict with each other. There are three possible "outcomes" of such situations, namely 1. actual double localization, that is, diplopia, 2. dominance of the stronger mode of localization over the weaker one (subordination of the latter to the former), and 3. a compromise. All three phenomena may be observed in cases of strabismus. In the beginning, particularly in a paralytic case, there is double vision but soon the situation changes to subordination of one eye, that is suppression. This, during early childhood, may lead to amblyopia and eccentric fixation. There is, however, the possibility of the squinting eye "liberating itself from the state of subordination and resuming independent, correct localization." When this happens suppression becomes superfluous. The two eyes localize correctly despite the abnormal motor condition; the state of harmonious anomalous correspondence has been reached. In some cases the dependent and the independent mode of localization battle with each other for a while but finally a compromise may be reached in the form of nonharmonious anomalous correspondence.

The term "false projection" for anomalous correspondence is poorly chosen because, actually, patients with harmonious anomalous correspondence localize correctly. Peter C. Kronfeld.

Colenbrander, M. C. **What do we see straight?** Ophthalmologica **132**:291-294, Nov., 1956.

Some of the architectonic features of the Parthenon in Athens are interpreted as indications that the old Greek architects were familiar with and consciously or unconsciously used optical illusions to produce certain psychologic and aesthetic effects. The architrave which looks perfectly straight to the observer is slightly arched upwards. The columns taper imperceptibly upwards which conveys the impression of greater than actual height. The corner columns which are usually viewed against the darker sky which, by irradiation, makes them seem narrower, are actually wider than the other columns. The floor of the Parthenon bulges slightly upwards, which creates the impression of firmness. "Indeed, the unprejudiced knowledge of the human mind which is so clearly shown in this majestic building (the Parthenon), is awe-inspiring." Peter C. Kronfeld.

Garzino, Alessandro. **Modification of the collagen fibers in malignant myopia.** Rassegna ital. d'ottal. **25**:241-280, July-Aug., 1956.

Electron microscopy demonstrates that the collagen fibers from the myopic staphyloma have fibers much reduced in size. There is an indication that the fibers have developed in a condition of decreased nutrition. Both microscopic and histologic study are convincing of the defective nutrition of the staphylomatous tissue. The latter shows the fibers narrower than normal and more widely spaced and the cement substance more abundant. Study of the histology of the fetal sclera at five months and at nine months show increasing size of the fibers as fetal life progresses. The pathologic changes suggest a defect in fibrogenic activity, either prenatal or postnatal. The article is well illustrated. (12 figures, 149 references) Eugene M. Blake.

Muinos Simon, Alfredo. **The present status of treatment for amblyopia.** Arch. Soc. oftal. hispano-am. **16**:1195-1210, Nov., 1956.

This is chiefly a description of Cüpper's method of macular reeducation with the euthyscope, and of Bangerter's method of pleoptic training. The author reports statistically 42 cases of amblyopia treated with the euthyscope, the patients ranging between 5 and 40 years of age. (1 table) Ray K. Daily.

Sachsenweger, R. and Junker, B. **The stereoscopic vision of children with normal sight.** Ophthalmologica **132**:109-115, Aug., 1956.

The measurements of stereoscopic acuity reported in this paper are intended to serve as basic data or "controls" in the evaluation of the results of the various forms of treatment of sensory-motor anomalies in children. The stereoscopic acuity of 217 boys and girls with ages ranging from 6 to 11 years, good visual acuity in each eye and without motor anomalies was estimated by means of Hering's drop test and a modified Howard-Tolman test. The latter test was more revealing than the former. The stereoscopic acuity increases up to the age of nine years at which time the full normal acuity is reached. The child's ability to concentrate is also a significant factor. (3 figures, 13 references)

Peter C. Kronfeld.

5

DIAGNOSIS AND THERAPY

Abalikhin, A. **An apparatus for localization of intraocular foreign bodies.** Vestnik oftal. **1**:37-40, Jan.-Feb., 1957.

Abalikhin describes his new simplified apparatus; it can be used in the X-ray room for the localization of a foreign body and it also can be used in the operating room, so that the surgeon can see exactly the location of the foreign body. No additional calculations are necessary, the distance is indicated on the arcs of the apparatus. (1 drawing, 1 table)

Olga Sitchevska.

Bangerter, A. **Nylon thread implants after enucleation or evisceration.** Ophthalmologica **132**:264-270, Oct., 1956.

Crocheted nylon thread balls make satisfactory implants after enucleations and eviscerations. The loose spongy material is readily accepted and well tolerated by the orbital tissues. (13 figures)

Peter C. Kronfeld.

Boet, D. J. **Clinical results with phosphoryl choline calcium.** Ophthalmologica **132**:150-152, Sept., 1956.

Clinical trial of topically administered phosphoryl choline calcium (the N. V. Philips-Roxane Company in Amsterdam) in about 20 cases of posttraumatic or postinflammatory ocular hypotony suggests that the drug has a beneficial pressure-raising effect and is free of harmful side-effects.

Peter C. Kronfeld.

Bohlig, H. **Film holder for bone-free X rays.** Klin. Monatsbl. f. Augenh. **130**: 378-380, 1957.

This holder allows the dental film to be firmly pressed into the orbit. The handle itself has a lead shell to protect the physician's hand. (4 figures, 3 references)

Frederick C. Blodi.

Curschmann, V. **Radiologic localization of intraocular foreign bodies.** Klin. Monatsbl. f. Augenh. **130**:381-385, 1957.

The contact glass of Comberg was modified. A fifth lead mark is placed at the anterior pole of the lens and this mark carries a small mirror parallel to the limbal plane. The mirror serves to get the eye into the right position. The light of an ophthalmoscope shines into the mirror and by its reflection the correct position can be obtained. This is an objective method and the eye may be deviating or even blind without influencing the accuracy of the result. (7 figures, 4 references)

Frederick C. Blodi.

Dikun, V. **Intrachamber forceps for the removal of amagnetic foreign bodies from the eye.** Vestnik oftal. **1**:42-43, Jan.-Feb., 1957.

A new forceps for the removal of amagnetic foreign bodies from the anterior

chamber and the vitreous is described in detail. The advantage of the forceps, which was made from syringe needles, is that little aqueous is lost during the introduction of the forceps and the foreign body is more easily grasped in the chamber with a nearly normal depth. (1 drawing) Olga Sitchevska.

ten Doesschate, J. **The ophthalmologist's attitude toward the orthorater.** Ophthalmologica **132**:282-284, Nov., 1956.

A number of orthoraters have been purchased and put into operation by industrial medical services in Holland. The Dutch ophthalmologists are likely to see in their offices referred patients with visual defects disclosed by the orthorater. "The ophthalmologist should take the findings obtained with the orthorater seriously and show by his attitude toward patients and orthorater technicians that he appreciates the interest which industry is showing in the visual health of the workers." The ophthalmologist should welcome mass visual screening programs with the orthorater because they may lead to the earlier detection of serious ocular diseases. Peter C. Kronfeld.

Goettsch, F. J. B. **Sterility of eyedrops.** Ophthalmologica **132**:167-171, Sept., 1956.

This study was prompted by an epidemic of corneal ulcers due to Bacillus pyocyaneous in the Rotterdam Eye Hospital. The source of the infection was found in contaminated ophthalmic solutions. The addition of phenylmercury nitrate (merphenyl nitrate N.N.R.) to ophthalmic solutions and of zephiran to the saline used for irrigations, both in concentrations of 1:25,000, proved an effective measure to maintain sterility of the solutions. Other antiinfective and preservative agents suitable for ophthalmic solution are chloroform (4 drops per 10 ml. of solution) and nipagin (methyl-p-hydroxybenzoate). Peter C. Kronfeld.

Gualdi, G. and Tusini, A. **Histologic study of the anterior segment of the eye after prolonged treatment with cortisone.** Rassegna ital. d'ottal. **25**:180-185, May-June, 1956.

Ten rabbits were subjected to local application of cortisone for periods of 60 and 90 days. One percent cortisone in ointment form was placed in the conjunctival sac four times daily and the eyes were removed for histological study. There was no actual damage to the various layers of the cornea or the iris. The author therefore concludes that the fear that prolonged use of cortisone in the conjunctival sac is harmful is unfounded. (4 figures) Eugene M. Blake.

Henkes, H. E., van der Tweel, L. H. and Denier van der Gon, J. J. **Selective amplification of the electroretinogram.** Ophthalmologica **132**:140-150, Sept., 1956.

Compared to existing subjective methods of testing retinal functions, electroretinography has the disadvantage of being very much less sensitive. Henkes and his associates have attempted to partially correct this weakness of the method by selective amplification, that is by using intermittent, rhythmic stimuli and by introducing into the electric circuit an amplifier tuned to the frequency of the stimuli. Such a setup amplifies principally the electric responses coming from the retina, and, in a sense, purifies the electroretinogram. The new method gives higher values, at least in the scotopic range, for the critical fusion frequency than the classical, direct method of electro-retinography. In cases of pigmentary degeneration with completely extinguished electroretinogram taken by the conventional method the method of selective amplification may yield definite positive responses. (9 figures, 7 references) Peter C. Kronfeld.

Hylkema, B. S. **A projection perimeter.** Ophthalmologica **132**:201-202, Sept., 1956.

The target light source of this perimeter is projected upon any desired area on the inner surface of a spherical segment of 35 cm. radius by means of a mirror mounted on the headrest, just above the eye to be examined. This mirror can be rotated by means of handles. The target light can be varied within wide limits and adapted to measurements of flicker photometry by interposing a rotating sectored disc. (2 figures)

Peter C. Kronfeld.

Hylkema, B. S. **Measurements of flicker fusion frequency in some ocular diseases.** Ophthalmologica **132**:202-203, Sept., 1956.

Measurements of the critical flicker fusion frequency (CFF) are a form of quantitative perimetry. Lesions in the retina or in any part of the visual pathway may affect the CFF. The author found the method particularly useful for the demonstration of early glaucomatous field defects and for the unmasking of malingerers. Peter C. Kronfeld.

Klecker, W. **Lashes in the anterior chamber.** Klin. Monatsbl. f. Augenh. **130**: 392-395, 1957.

In a 17-year-old boy a cilium could be extracted with a smooth capsule forceps. Early extraction is advised because of the danger of complication and infection. (7 references) Frederick C. Blodi.

Magdalena Castineira, Jaime. **Therapeutic results of streptokinase and streptodornase.** Arch. Soc. oftal. hispano-am. **16**: 1227-1235, Nov., 1956.

Experimental investigations on rabbits, and the results in five clinical cases lead to the conclusion that Varidase injected subcutaneously has no significant effect on the absorption of intraocular hemorrhages. In grave purulent processes of the anterior chamber or cornea this preparation reenforces the action of antibiotics, and has a very favorable influence on the resolution of the suppurative process. To illustrate the beneficial effect of Varidase, six cases of hypopyon and purulent keratitis treated with penicillin and Varidase are reported. (18 references)

Ray K. Daily.

Massimeo, A. **The association of hydrocortisone-oxytetracycline-tetracycline in ophthalmology.** Boll. d'ocul. **35**:560-568, Aug., 1956.

The author evaluated the efficacy of a combination of hydrocortisone-oxytetracycline-tetracycline in the treatment of corneal and conjunctival lesions. The results were satisfactory in those cases in which antibiotic and cortisone therapy is indicated. The results in herpetic infections were not encouraging. (2 figures, 6 references) William C. Caccamise.

Ohashi, K., Iizuka, T. and Momiki, H. **Studies on the ophthalmoscopic calipermicrometry and bifurcation angle measurement in retinal vessels.** Jikeikai Med. J. **3**:11-22, April, 1956.

These authors have modified Lobeck's method of measuring diameter of the arteriole by placing a caliper micrometer in the Gullstrand ophthalmoscope. The instrument projects an image on the retina so that the diameter can be measured within 0.01 millimeter (after adjustment of the figure for subject ametropia). In normal eyes at the disc edge, the temporal artery measured 0.112 mm., the nasal artery 0.096 mm. The temporal vein measured 0.142 mm., and the nasal vein 0.123 mm. The cold pressor test resulted in 8.7 percent constriction of the arteriole and 4.2 percent of the vein. With the hand in hot water, 35 percent of patients showed immediate dilatation and 65 percent of patients dilation after 10 minutes.

The vessels were measured in 67 patients before and after constant 50 grams bulbar compression. Effects of diathermy and various drugs in normal and diseased eyes are reported.

The angle of bifurcation was measured by the thread compass, and the peculiar requirements discussed. The angle varies as to type, and must be measured within certain distance limits of the bifurcation. The normal angle was found to be 65.4°, increasing to 69.1° in hypertension. After injection of adrenaline the angle widened 30 minutes. After calpinol, the angle narrowed 30 minutes of arc.

Paul W. Miles.

Pintucci, F. **Akinesia with curare in ocular surgery.** Boll. d'ocul. **35**:569-576, Aug., 1956.

The author discusses his technique in the use of curare for akinesia. Adequate preoperative sedation is emphasized. Such sedation together with punctuality in starting the operation permits the utilization of a minimum dose of curare. The results obtained in 186 ocular operations lead the author to believe that the advantages of akinesia with curare are as follows: absence of pain in the patient, accentuation of akinesia and hypotonia, and absolute reliability of effect. (28 references) William C. Caccamise.

Rosner, E. and Steinvorth, E. **The topical application of hydrocortisone in inflammations of the anterior segment.** Klin. Monatsbl. f. Augenh. **130**:372-378, 1957.

Good results were obtained in 100 patients, especially in those with iritis, iridocyclitis, phlyctenular keratoconjunctivitis, chronic blepharitis, marginal ulcers and disciform keratitis. It was superior to cortisone in five cases. (12 figures, 16 references) Frederick C. Blodi.

6

OCULAR MOTILITY

Rotter, H. **Oscillating recovery movements in alternating heterotropias.** Ophthalmologica **132**:116-124, Aug., 1956.

The paper concerns itself with pendulum-like, conjugate ocular movements which occur with shifts of fixation in patients with alternating heterotropia whose visual lines have been made parallel by prisms or surgery. In a case of alternating esotropia in which the angle of squint is "corrected" with prisms there is either no recovery movement at all as the eyes are alternatingly covered and uncovered, or there occurs the phenomenon of a jerky outward (abductive) movement of the eye taking over fixation, followed quickly by just as jerky an inward (adductive) movement. The eye that has given up fixation (behind the cover) follows the fixing eye in a perfect conjugated manner. The phenomenon has been known since Tschermak's description of his own alternating esotropia in 1899. Rotter gives a detailed analysis of the phenomenon in representative cases of alternating heterotropia and arrives at an explanation that links the phenomenon closely with the degree and type of anomalous correspondence. The more thoroughly this anomalous correspondence becomes established, the more pronounced is the oscillating recovery movement. For this interesting motor phenomenon Rotter suggests the term "Einstellschwankung" in German, "oscillation de mise au point" in French, and "side-jerk" in English. (5 references)

Peter C. Kronfeld.

Weekers, R., Moureau, P., Hacourt, J. and André, A. **Contribution to the etiology of concomitant strabismus and amblyopia: a study of identical and nonidentical twins.** Ophthalmologica **132**:209-229, Oct., 1956.

This study concerns itself with 15 pairs of twins and some of their ancestors which were subjected to thorough ophthalmological examination. The distinction between identical and nonidentical twins was made on the basis of the placental findings (where such findings were available), the degree of resemblance between the twins and their blood groups. Identi-

cal twins proved, with only one exception, identical with regard to their refractive errors. Heterotropia and amblyopia occurred, as a rule, in only one of the two identical twins. Strabismus and amblyopia are, therefore, considered complications of ametropia and not directly due to a genetic factor. "Consequently, the complete and precise correction of ametropia before school age seems to be an effective preventive measure against strabismus, amblyopia and alterations of the binocular functions." (22 figures, 2 tables, 11 references) Peter C. Kronfeld.

7

CONJUNCTIVA, CORNEA, SCLERA

ten Doesschate, J. **Corneal complications in lupus erythematosus discoides.** Ophthalmologica **132**:153-156, Sept., 1956.

In a case of histologically verified lupus erythematosus both corneas became involved in a chronic or recurrent superficial desquamating keratitis. The skin as well as the eye lesions improved on chloroquin treatment. (4 figures, 6 references)
Peter C. Kronfeld.

Flieringa, H. J. **Caterpillar hairs in the cornea.** Ophthalmologica **132**:187-188, Sept., 1956.

Two cases of caterpillar hairs in the cornea are reported. The first case was seen during the phase of punctate superficial keratitis due to multiple short hairs in the anterior stroma. A year later the eye was quiet and the hairs had disappeared from view. In the second case the gradual migration of the hairs from the superficial to the deeper corneal layers could be observed. Topical cortisone therapy kept the eye quiet.
Peter C. Kronfeld.

Flieringa, H. J. **Congenital corneal avitaminosis.** Ophthalmologica **132**:185-187, Sept., 1956.

A two-months-old baby girl, in bad nutritional state, was admitted to the eye clinic because of large bilateral congenital corneal leucomas. The baby's general condition improved rapidly on proper dietary measures. A penetrating keratoplasty was performed at the age of six months. The outcome of the operation is not given. The leucomatous disc removed at operation showed histologic changes compatible with the diagnosis of vitamin A deficiency.
Peter C. Kronfeld.

Gibson, J. B. G. **Brisbane survey of pterygium.** Tr. Ophth. Soc. Australia **16**: 125, 1956.

Various techniques are reviewed and the results of 1,000 operations are analysed. Without radiation the recurrence rate varied from 20 to 30 percent. Contact X-ray irradiation was very valuable in preventing recurrences; the rate fell to 10 percent. After four years small lens opacities were sometimes found but none interfered with vision. Ronald Lowe.

Gualdi, G. and Tusini, A. **A case of osteoma of the bulbar conjunctiva.** Boll. d'ocul. **35**:577-586, Aug., 1956.

The authors report a case of osteoma of the bulbar conjunctiva in a 10-year-old boy. A thorough review of the literature revealed only 15 cases. The authors conclude that this lesion occurs primarily in young patients and that its most frequent location is in the upper outer sector of the bulbar conjunctiva. The lesion is considered to be congenital in nature. (4 figures, 21 references)
William C. Caccamise.

Jager, H. **Nonpigmented cystic nevus of the conjunctiva.** Ophthalmologica **132**: 195-196, Sept., 1956.

A gray nevus of the bulbar conjunctiva near the limbus, present since birth, started to grow when the patient reached the age of 14 years. The tumor was excised and proved to be a typical nonpig-

mented cystic nevus, without any signs of malignant transformation. (2 figures)

Peter C. Kronfeld.

Kerkenezov, N. **A pterygium survey of the far north coast of New South Wales.** Tr. Ophth. Soc. Australia **16**:110, 1956.

Statistics for the incidence of pterygia on the far north coast of New South Wales are presented and indicate that pingueculae and pterygia are essentially the same disease. Causative factors are 1. exposure of the eyes to the ultraviolet rays, 2. heredity. Ronald Lowe.

Latte, Bachisio. **Evaluation of the activity of antibiotics upon the trachoma virus.** Rassegna ital. d'ottal. **25**:193-201, May-June, 1956.

Latte studied 104 boys between the ages of 6 and 12 years to determine the efficacy of the antibiotics against trachoma. In all instances the inclusion bodies were found and stained; the initial bodies, inclusion bodies and the elementary corpuscles were identified. One eye of each patient was treated with antibiotics, aureomycin, terramycin and chloramphenacol in ointment form six time a day. Twice a day material was studied for the presence of the virus, rubbing and scarifying the palpebral conjunctiva and the cul-de-sac. The virus rapidly disappeared under this treatment. However, experimentation in a blind child by instilling material from fully treated trachoma was negative. (6 references)

Eugene M. Blake.

Mann, I. **More about trachoma.** Tr. Ophth. Soc. Australia **16**:64, 1956.

The author has conducted population surveys for ophthalmic disease in three areas of Western Australia and in New Guinea. Trachoma was the most important disease found. Some areas showed high virulence, others low. Almost all types of climate were encountered so that climate can be no significant factor. The disease is spread by personal contact especially in children. Its severity is enhanced by secondary infection. Treatment of school children gives the best chance of eradicating the disease. Personal hygiene needs to be taught to the children at the same time. (7 tables)

Ronald Lowe.

Manschot, W. A. **The corneal ring of Kayser and Fleischer.** Ophthalmologica **132**:164-166, Sept., 1956.

Postmortem examination in a typical case of hepatolenticular degeneration with corneal rings (Wilson's disease) showed severe cirrhosis of the liver. The peripheral portions of Descemet's membrane contained pigment granules with the staining characteristics of copper salts. (1 figure, 2 references)

Peter C. Kronfeld.

Mead, K. W. **Beta radiation for recurrent pterygia.** Tr. Ophth. Soc. Australia **16**:101, 1956.

Beta radiation is the ionising radiation of choice. Radium D applicators are best but are difficult to obtain and a strontium 90 applicator is used. A ring-shaped holder allows accurate localisation. The average dose is 2400 r. in a single application. There is no need for fractionation of the radiation. Ronald Lowe.

Mortelmans, Luc. **A case of oculoglandular syndrome due to Newcastle virus.** Ophthalmologica **132**:105-108, Aug., 1956.

An acute conjunctivitis of the Parinaud type in a 50-year-old chicken farmer was shown to be due to Newcastle virus by 1. typical pathologic findings in some chickens the patient was raising, 2. a mild febrile systemic disease preceding the conjunctivitis, and 3. a very high titer of specific agglutinins in the patient's blood. (6 references) Peter C. Kronfeld.

von Nordheim, R. W. **The treatment of superficial punctate and dendritic keratitis with naphazoline.** Ophthalmologica **132**:198-200, Sept., 1956.

Frequent instillations of privine hydrochloride in 0.5 or 1 percent solution are reported to be effective in the treatment of the corneal conditions stated in the title. Superficial punctate keratitis responded very promptly, but recurred if the treatment was stopped abruptly. The recurrences were just as responsive to privine therapy as the first attack. Antibiotics were used concurrently only if there were signs of a bacterial infection or if marked photophobia made the wearing of an eye patch necessary. (7 references)

Peter C. Kronfeld.

Redmond, K. B. **Pterygia in western New South Wales.** Tr. Ophth. Soc. Australia **16**:120, 1956.

114 operations were performed of which 77 percent were satisfactory, 13 percent slightly unsatisfactory, 10 percent very unsatisfactory. Ronald Lowe.

Sigtenhorst, M. L. and Gingrich, W. D. **Bacteriologic studies of keratitis.** South. M. J. **50**:346-350, March, 1957.

Trauma or degenerative conditions of the cornea are essential in the etiology of infective keratitis. The most common organisms found were Pseudomonas aeruginosa, Proteus mirabilis, Micrococcus pyogenes aureus, and the pneumococcus.

Three cases of mycotic corneal ulcer are reported. They were caused by Nocardia species, Scopulariopsis, and Fusarium. (2 tables, 10 references)

Irwin E. Gaynon.

Sysoyev, F. **Current problems of combating trachoma.** Vestnik oftal. **2**:6-15, March-April, 1957.

About 50 percent of the population in the Udmurt region (Ural Mountains) was affected with trachoma which resulted in blindness in 4,000 people in 1925 to 1930. By 1950 only 6 percent of the rural population had trachoma, and by 1956 92.2 percent of the population was cured.

The author also discusses the criteria on which one considers a patient "cured" from trachoma. He studied 1,000 cases of trachoma, grade 4, and the recurrence of the disease. His opinion is that any recurrence of trachoma is an indication that the cure was not complete and he concludes that the practical criteria for judging the cure of trachoma need further study. (3 tables) Olga Sitchevska.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

ten Doesschate, J. **A free pigmented cyst in the anterior chamber.** Ophthalmologica **132**:284-285, Nov., 1956.

In the otherwise normal left eye of a 22-year-old man a round brown body usually occupied the six-o'clock position in the chamber angle, but could be made to move toward 3 or 9-o'clock by tilting the patient's head plus gentle massage through the cornea. Such loose bodies in the anterior chamber are either detached flocculi or remnants of the pupillary membrane. They cause no symptoms and require no treatment. (2 figures, 4 references) Peter C. Kronfeld.

Illingworth, R. S. and Lorber, J. **Tubercles of the choroid.** Arch. Dis. Childhood **31**:467-469, Dec., 1956.

The authors distinguish four stages in the development of choroidal tubercles. The earliest stage is manifest as a rounded yellowish area which is not elevated. The lesions are much smaller than the disc and there may be 10 to 20 in each eye. In the second stage the outline becomes more distinct. In the next stage the tubercle becomes still paler, eventually parchment white and outlined with pig-

ment. In the last stage the entire area becomes densely pigmented. Most early tubercles remain in the first stage for about four weeks and occasionally remain "early" for several months. Smaller tubercles may remain in the second stage for years and finally disappear entirely. The larger ones progress to stage three in three months or so. The last stage appears after three or four years. (4 figures, 1 table, 8 references) F. H. Haessler.

Manschot, W. A. **Hyaline membrane on the anterior surface of the iris.** Ophthalmologica **132**:160-162, Sept., 1956.

Extension of the corneal endothelium and of a Descemet-like hyaline membrane on the anterior surface of the iris was found histologically in one case of absolute glaucoma after blunt injury and one case of atrophy of the globe of undetermined cause. (5 figures)

Peter C. Kronfeld.

Pau, H. **Choroidal detachment.** Klin. Monatsbl f. Augenh. **130**:347-371, 1957.

This is not a true detachment, but a marked, often circumscribed, edema of the choroid. The author therefore suggests the name "spongiosis." Pigment disturbances in the retina may result. The globe is always extremely soft. Two main types exist; one is associated with a flat chamber and follows an operation on the anterior segment and the other follows a disease or surgery of the posterior segment. It is an inevitable complication of vitreous loss. The anterior chamber is here very deep and filled with a protein-rich fluid. There is also an edema of the ciliary body. This was found in rabbits in which this type of choroidal detachment was produced by a posterior sclerectomy. (23 figures, 35 references)

Frederick C. Blodi.

Remky, H. **Aqueous findings as a basis for the nonspecific treatment of uveitis.** Klin. Monatsbl. f. Augenh. **130**:335-347, 1957.

In every case of uveitis (230 patients in 3 years) an aqueous analysis was made with cytologic evaluation and determination of the proteins. The influence of cortisone, fever and vitamin D_2 on the cells and globuline in the aqueous are discussed. (12 figures, 2 tables, 10 references) Frederick C. Blodi.

9

GLAUCOMA AND OCULAR TENSION

Agarwal, L. P. and Saxena, R. P. **General changes in glaucoma.** Ophthalmologica **132**:258-263, Oct., 1956.

Observations on 35 cases of glaucoma and ten normal controls lead the authors to believe that there are differences between the two groups with regard to the diurnal fluctuations of the venous blood pressure and the degree of hemodilution and the capillary fragility during the water-drinking test. These systemic differences may be eliminated by a successful, that is tension-normalizing, glaucoma operation. The authors suggest that some of the systemic abnormalities in glaucoma are due to "liberation of a toxin that is absorbed in the circulation and brings about the general changes." (1 table, 17 references)

Peter C. Kronfeld.

Arkhangelsky, V. **Diathermy coagulation of the sclera in the region of the ciliary body in glaucoma.** Vestnik oftal. **2**:15-22, March-April, 1957.

During the last three years, experimental and clinical work was done by Arkhangelsky and his coworkers at the 1st Moscow Medical Institute. There were 111 patients under observation for two years and the author describes his method of the operation.

The conjunctiva is incised near the attachment of the superior rectus muscle

and three sutures are placed near the incision. A neutral electrode is attached to the shoulder of the patient and with a blunt, round electrode, 1 mm. in diameter, six to eight diathermy coagulations, 2 mm. apart, are applied to the sclera for 2 to 4 seconds, above the transparent edge of the limbus between 10 and 2 o'clock; the strength of the current is 35 to 50 MA. About 2 mm. above the first, a second row of coagulations is made. Since the intraocular pressure rises after the coagulation of the sclera, a paracentesis of the sclera, 5 mm. long, is done by keratome incision in front of the first row. The posterior edge of the sclera is pressed by a spatula; by this procedure the aqueous escapes and the eye becomes soft. There is usually no prolapse of the iris as its root is adherent and the angle of the anterior chamber is obliterated. Should the prolapse occur, the iris is pushed back into the anterior chamber with a spatula.

Arkhangelsky stresses the importance of the size of the electrode; it should be 1 mm. in diameter as it penetrates the thickness of the sclera (1 mm.) and thus its action spreads to the ciliary body and fewer coagulations can be made. In all but five patients with advanced glaucoma who were operated upon because the tension could not be normalized by miotics, the tension remained normal; in some the visual fields and vision improved. (3 drawings) Olga Sitchevska.

Cavka, V. **A control center for the intraocular pressure located in the frontal lobe.** Ophthalmologica **132**:76-86, Aug., 1956.

The author's assumption of a regulatory center for the intraocular pressure in the frontal lobe is based on two sets of observations, namely slight fluctuations of blood pressure and ocular tension following frontal lobotomy or lobectomy in schizophrenics and the encephalographic finding of slightly dilated subarachnoidal spaces over the frontal and parietal lobes in four cases of primary glaucoma. (6 figures, 7 references) Peter C. Kronfeld.

Flieringa, H. J. **Internal iridencleisis.** Ophthalmologica **132**:190-194, Sept., 1956.

Flieringa's operation is a cyclodialysis through a trephine opening 6 to 7 mm. behind the limbus combined with the subscleral iridencleisis of Raeder (cfr. Mauksch in Arruga's Ocular Surgery). Peter C. Kronfeld.

Flieringa, H. J. **A modified method of goniotomy.** Ophthalmologica **132**:188-190, Sept., 1956.

For congenital glaucoma Flieringa makes incisions of the chamber angle with a special, small-tipped cataract knife, with accurate fixation of the globe by means of bridle sutures under all four rectus muscles and without a contact lens. "During the operation the abnormal connections between iris and posterior surface of the cornea are seen to burst apart." The tension was normalized by one such goniotomy in seven out of eight consecutive cases. Peter C. Kronfeld.

François, J. **Gonioscopy in primary glaucoma.** Tr. Ophth. Soc. Australia **16**: 13, 1956.

The author emphasises that simple glaucoma and closed-angle glaucoma are two totally different and independent disease entities which have nothing in common and should not be studied together. Gonioscopy is necessary to avoid confusion. In simple glaucoma there is no relation between the degree of opening of the angle and the ocular hypertension. There are statistical differences between normal angles and those in simple glaucoma but these cannot be distinguished gonioscopically in individual cases. The most minute gonioscopic examination does not reveal any specific manifestations in simple glaucoma.

The diagnosis of closed-angle glaucoma is not based on the narrowness of the angle but on its closure during elevated tension. The closure of the angle precedes and is the cause of the elevation of tension. Goniosynechiae form rapidly and may prevent a return to normal. Blocking of the angle is favoured by its narrowness but an angle may be narrow and remain so without ever giving rise to glaucoma. The true origin is a neurovascular disturbance, probably in the diencephalon.
Ronald Lowe.

Goedbloed, J. **The prognosis of simple glaucoma.** Ophthalmologica **132**:181-184, Sept., 1956.

Eight cases are reported in which the diagnosis of chronic simple glaucoma was made and treatment instituted at a time when visual acuity and visual fields in one eye were still practically normal but very markedly reduced in the other eye. During five years of treatment and observation the near-normal eyes showed no loss of function while in their mates the disease showed further progression. The conclusion is drawn that in chronic simple glaucoma the prognosis is fairly favorable when the visual field is yet unaffected and the visual acuity still normal. The diagnosis of chronic glaucoma has to be made before the development of the characteristic visual field defects. (8 references) Peter C. Kronfeld.

Jucenda Avello, J. **The venous ocular pressure in the pathogenesis of simple glaucoma.** Arch. Soc. oftal. hispano-am. **16**:1211-1218, Nov., 1956.

This is a report of an investigation of the venous pressure in glaucoma, with the objective of adding data for the solution of the disagreement as to the pathogenesis of simple glaucoma. The data of the investigation shows, statistically and graphically, that the venous episcleral pressure is somewhat below normal in simple glaucoma. This diminution is attributed chiefly to the diminished quantity of blood and aqueous reaching the veins. The diminished venous pressure holds an inverse relation to the resistance to aqueous outflow, which supports the mechanical theory of pathogenesis of simple glaucoma. An increase in venous pressure was never encountered in simple glaucoma. It is possible that a general rise of venous pressure may provide slight changes in intraocular pressure; these are, however quite different from the glaucomatous picture. (2 graphs, 2 tables, 9 references) Ray K. Daily.

Kurlander, Arnold B. **Glaucoma: a public health problem.** Tr. Am. Acad. Ophth. **60**:774-777, Nov.-Dec., 1956.

The author, a public health officer, outlines briefly what is important in detecting more cases of glaucoma: 1. a mass screening program, 2. tonometry as a part of every general physical examination and 3. community interest and action enlisted through demonstration projects and financial support. There are 59 million Americans over 40 years of age.
Theodore M. Shapira.

Matsumoto, T. **Tension-lowering mechanism of iridencleisis.** Acta. Soc. Ophth. Japan **61**:265-282, March, 1957.

Matsumoto demonstrated histologically that in rabbits an anastomosis between the uveal and conjunctival blood vessels develops after iridencleisis and a filtration cicatrix also occurs. The filtration cicatrix was demonstrated by a fluorescein test. (15 figures, 4 tables, 54 references)
Yukihiko Mitsui.

Matteucci, Pellegrino. **Study of the apparently normal eye in unilateral simple glaucoma.** Rassegna ital. d'ottal. **25**:161-172, May-June, 1956.

The author followed the diurnal tonometric curve, angioscotometry pupil-

lography and provocative tests in four cases of unilateral glaucoma. His studies led him to believe that diurnal tension curves and pupillography show the earliest changes in the "normal eye" and that the uveal membrane is the probable seat of the first functional lesions. (8 figures, 21 references) Eugene M. Blake.

Miyata, N. **A study of aqueous veins. II-III.** Acta Soc. Ophth. Japan **61**:164-171, 253-264, Feb., March, 1957.

Miyata studied neoprene casts of aqueous veins in human eyes. He used one normal eye removed because of retrobulbar tumor, one eye with acute congestive glaucoma, one eye with secondary glaucoma and another eye with glioma of the retina. In glaucoma there was little change in the neoprene casts of Schlemm's canal and the outflow ducts. He also made clinical observations of the aqueous veins in glaucoma. He concludes that the compensation maximum has little value in the diagnosis of glaucoma, and that the glass rod phenomenon and the compensation maximum do not seem to be influenced definitely by the diurnal variation of the ocular tension. Finally, he examined the aqueous veins in postoperative glaucoma and concluded that cyclodialysis may reduce the resistance against the aqueous outflow while the iridencleisis does not seem to have this effect. (7 figures, 10 tables, 56 references)

Yukihiko Mitsui.

10

CRYSTALLINE LENS

Colenbrander, M. C. **Lenticular sclerosis and age.** Ophthalmologica **132**:289-290, Nov., 1956.

Routine measurements of visual acuity are made under conditions of optimal or near optimal illumination and contrast. Tested in this manner, the visual acuity shows very little variation with age despite the very much lesser degree of transparency of the lens in the older age groups. The explanation of this apparent discrepancy is that lenticular sclerosis reduces principally the contrast between dark and light objects. Since that contrast between optotypes and background is almost maximal in routine vision tests a slight or even moderate degree of nuclear sclerosis may not affect the outcome of the test. Distinction between less contrasting dark and light objects is, however, of vital importance in the case of operators of passenger automobiles or trucks. The author has designed a handy little instrument for the estimation of visual acuity under conditions of reduced contrast. Peter C. Kronfeld.

Gemolotto, Guglielmo. **Anterior and posterior copper cataract.** Arch. di ottal. **60**:271-281, Sept.-Oct., 1956.

A copper splinter in the vitreous had caused an anterior sunflower cataract and a starlike opacity in the posterior capsule. The pertinent literature is reviewed. (3 figures, 26 references) John J. Stern.

Schröder, G. **The X-ray picture of a calcareous cataract.** Klin. Monatsbl. f. Augenh. **130**:385-388, 1957.

A patient, 73 years old, with characteristic X-ray picture in the left orbit is described. (1 figure, 42 references)

Frederick C. Blodi.

Shipman, J. S. and Luce, C. M. **Recent advances in cataract surgery.** Rocky Mt. M. J. **54**:3, 242-251, March, 1957.

A very complete description of the historic background, the evolution, and the methods in general use is given.

Irwin E. Gaynon.

11

RETINA AND VITREOUS

Asayama, R., Sakaue, E. and Tanaka, S. **Results of surgery in detachment of**

the retina. I-II. Acta Soc. Ophth. Japan **61**:123-136, 207-223, Feb., March, 1957.

This is a statistical analysis of the results of surgery for retinal detachment in 244 eyes. The condition was found in about 1.7 percent of the outpatients, was idiopathic in 93 percent and traumatic in 7 percent; 64 percent occurred in males and 36 percent in females. About 55 percent of the detachments were in myopic eyes and an excessive myopia was found in about 20 percent of the cases. In 89 percent of the cases tears were found; surgery was successful in 77 percent of the early cases (seen one month after onset) but in only 66 percent of late cases. The results in eyes without tears and in aphakic eyes were poor in general; the success was 39 percent and 25 percent respectively. Recurrence was seen in 3 percent of the cured cases. (1 figure, 25 tables, 19 references) Yukihiko Mitsui.

Babel, J. and Ziv, B. **Histologic and electroretinographic study of experimental retinal degenerations.** Ophthalmologica **132**:65-75, Aug., 1956.

In the experimental animal a number of chemical agents have been known to cause retinal degeneration resembling human retinitis pigmentosa. The effects upon the retina of the rabbit of four such agents, sodium iodate, sodium monoiodoacetate, sodium fluoride and glycerinaldehyde were studied ophthalmoscopically, electroretinographically and histologically. Sodium iodate was found to cause a slowly progressive degeneration with electroretinographic and histologic manifestations very closely resembling retinitis pigmentosa in man. Sodium monoiodoacetate acted much more rapidly; the retina became markedly edematous and the b-wave of the electroretinogram was wiped out a few minutes after the first intravenous injection of the drug. Sodium fluoride and glycerinaldehyde had no anatomic effect and only transient effect on the electroretinogram. (cfr. Noell, Am. J. Ophth. 35:126, 1952 and 36:103, 1953). (6 figures, 16 references) Peter C. Kronfeld.

Bignell, J. **The detached retina.** Tr. Ophth. Soc. Australia **16**:36, 1956.

The points emphasised are: 1. the retina should be demonstrated ophthalmoscopically to be in position at the end of operation and the amount of lamellar scleral resection is judged from the amount of subretinal fluid present; 2. closure of the hole by diathermy is performed after the retina is in place and 3. the value of a dependent position of the hole after the operation depends on the absence of subretinal fluid and also upon a radical posturing of the patient in bed.

Ronald Lowe.

Dorsello, U. and von Berger, P. **Bilateral retrolental fibroplasia in identical twins.** Rassegna ital. d'ottal. **25**:173-179, May-June, 1956.

Retrolental fibroplasia in both eyes is reported. Only two similar cases have been described. In one twin one eye was of normal size while the other was buphthalmic. (11 references)

Eugene M. Blake.

Favre, M. and Goldmann, H. **Posterior detachment of the vitreous.** Ophthalmologica **132**:87-97, Aug., 1956.

For several years the authors have been engaged in systematic biomicroscopic studies of the normal and diseased vitreous with the aid of Goldmann's triple-mirror contact glass. The normal biomicroscopic appearance is dominated by alternating dark and bright bands or stripes which run parallel to Cloquet's canal. Toward the periphery the bright stripes coalesce and terminate in the region of the vitreous base. Degenerative changes may be recognized in most eyes between the ages of 40 and 50 years and

considerably earlier in myopes. Most commonly the degeneration occurs in the form of cavities and delicate but distinct fibrils instead of the normal broad bands. "Fibrillar destruction" is the term suggested by the authors. Gradually the cavities increase in size and finally the posterior hyaloid separates from the retina. This latter change may occur suddenly as the result of a break in the posterior wall of a large cavity. Through this break a large amount of vitreous fluid is suddenly transferred from an intravitreal cavity to a retrovitreal space. (10 figures, 8 references) Peter C. Kronfeld.

Hart, J. **Shallow peripheral retinocele.** Tr. Ophth. Soc. Australia **16**:135, 1956.

Routine peripheral field charting occasionally shows small defects due to retinoceles. The following clinical features are noted: clear vitreous, no hole, one or perhaps two dark veins, a peau d'orange effect, striations, and glittering, silvery spots. The condition does not seem to be progressive. Ronald Lowe.

Hoppenbrouwers, R. **Rare anomalies of the fundus.** Ophthalmologica **132**:131-133, Sept., 1956.

Under the title of rare fundus anomalies the author presented four case reports at the annual meeting of the Netherlands Ophthalmological Society in May, 1955. The reports concerned 1. a case of Hodgkin's disease with extensive retinal hemorrhages which cleared on combined streptomycin-paraaminosalicylic acid treatment; 2. a case of bilateral grouped pigmentation of the retina; 3. a case of renal hypertension with predominant sclerosis of the choroidal vessels (Siegrist's spots) and 4. a case of dermatomyositis with transient, recurrent, fluffy retinitic spots. (7 figures) Peter C. Kronfeld.

Kastner, M. **Observations on premature infants.** Klin. Monatsbl. f. Augenh. **130**:304-310, 1957.

Among 130 infants was one child with partial retrolental fibroplasia. The secretion of tears is reduced in these children and this may explain the occasional poor visibility of their fundus. (23 references) Frederick C. Blodi.

Manschot, W. A. **Difficulties in the clinical diagnosis of retinoblastoma.** Ophthalmologica **132**:162-164, Sept., 1956.

In only eight out of 15 eyes enucleated on the suspicion of retinoblastoma did the histologic examination reveal a malignant neoplastic disease. The pathologic findings in the other cases were cicatricial retrolental fibroplasia in two, angiomatosis of the retina, microphthalmos with choroidal coloboma, synechiae between lens and cornea in one each, and retinal detachment of undetermined cause in two eyes. Despite the high percentage of incorrect clinical diagnoses in this series the enucleation, in the author's opinion, is indicated and justifiable in the clinically suspicious cases if the vision is irreparably lost. Manschot stresses the point made by A. B. Reese that retinoblastoma never occurs in a microphthalmic eye. (6 figures) Peter C. Kronfeld.

Patz, Arnall. **Role of oxygen in retrolental fibroplasia.** Pediatrics **19**:504-524, March, 1957.

For his researches on retrolental fibroplasia, Dr. Patz received the E. Mead Johnson scroll and $1000. After the presentation, he reviewed the subject of oxygen and retrolental fibroplasia. Both clinical and experimental studies showed clearly that excessive oxygen is an important and probably the principal factor in RLF. The fibroplasia is due to oxygen susceptibility in tissues immaturely vascularized. Duration of oxygen exposure was the most important single factor. The first stage was vasoconstriction and obliteration, followed by proliferation. (20 figures, 2 charts, 1 table, 37 references) Paul W. Miles.

Spitsin-Yakubovsky, K. **Lesion of the retina in physical exertion.** Vestnik oftal. 1:36-37, Jan.-Feb., 1957.

A man, aged 22 years, noticed loss of vision of the lower half of the eye after lifting a heavy load. There was decreased sensitivity of the skin in the area of the first and second branches of the trigeminus. The upper temporal quadrant of the retina was opaque milky-gray; the lower border of this opacity was just above the macula and the disc. The vision was reduced to 0.1 and there was loss of the lower half of the visual field. After bed rest for 24 days and intravenous glucose injections, the vision was restored to normal. The lesion in the retina was barely noticeable, and there was only a relative scotoma in the lower part of the field. A month later the patient was readmitted to the hospital and although there were no visible changes in the retina, there was complete loss of the lower half of the visual field.

Olga Sitchevska.

Valvo, Giuseppe. **A case of Coats' retinitis.** Arch. di ottal. 60:199-218, July-Aug., 1956.

After discussion of the literature, a case of Coats' disease in a 17-year-old girl is presented. Enucleation was performed because of secondary glaucoma. Vascular changes consisted of numerous ectatic, tortuous retinal vessels with hemorrhages. More important are the changes of retina and pigment epithelium where there were vacuoles, larger toward the posterior pole and filled with an acidophile fluid. Proliferation of glial tissue, which is considered secondary to the vascular changes, was also observed. The choroid was hypertrophic in some places and atrophic in others, with many congested capillaries and thromboses. A uniform gelatinous mass was found between the pigment epithelium and the nerve fiber layer of the retina. The condition is considered to be due to vascular changes of retina and choroid. These changes are partly of an atrophic, partly of a reactive proliferative character. The primary cause of this disease, however, is not known. (10 micrograms, 26 references) John J. Stern.

12

OPTIC NERVE AND CHIASM

De Simone, S. **Retrobulbar optic neuritis during psoriasis.** Arch. di ottal. 60: 257-270, Sept.-Oct., 1956.

Two patients developed retrobulbar neuritis during an exacerbation of psoriasis. Complete recovery took place under treatment with novaneurine, cilotropine vitamin B_1, chinofenile and extraction of teeth with caries. The author discusses the current theories of psoriasis as a microbic, viral, dysmetabolic, allergic or a collagen disease and tries to relate these theories to the genesis of retrobulbar neuritis. (35 references)

John J. Stern.

Heer, Giuseppe. **Roentgen therapy of optic neuritis.** Rassegna ital. d'ottal. 25: 220-223, May-June, 1956.

Heer poses two questions: 1. is the treatment of optic neuritis by irradiation with X-rays justifiable, and 2. is the improvement obtained by this therapy the result of modifications produced by the X-rays? Treatment with radiation plus antibiotics gives better results than antibiotics alone. This is judged by improvement in acuity and fields of vision. As to the etiology of the neuritis, six cases were due to sinus disease, 13 retrobulbar lesions were probably of virus origin, four with symptoms of demyelinating and eight were caused by alcohol-tobacco poisoning. The least improvement was seen in the neuritis due to sinus infection and to alcohol-tobacco poisoning. (3 references) Eugene M. Blake.

13

NEURO-OPHTHALMOLOGY

ten Doesschate, J. **Electronystagmographic recording of a case of monocular vertical nystagmus.** Ophthalmologica **132**:156-159, Sept., 1956.

The report concerns a 59-year-old woman whose unilateral vertical nystagmus was first discovered in the course of a routine slitlamp examination. Two independent pathologic conditions were present, namely bilateral chronic simple glaucoma, far advanced in the left eye and moderately advanced in the right, and paralytic convergent squint of the left eye due to a lateral rectus paralysis following a fall from a bicycle six years before. A tenotomy of the left medial rectus performed three years after the accident had reduced the angle of squint but had not eliminated the diplopia. The patient, therefore, wore a frosted lens over the left eye. The nystagmus became most noticeable with both eyes open and the right eye fixating. Close observation of the right eye during the nystagmic excursions of the left eye revealed not the slightest movement of the globe but very slight rhythmic elevations of the upper lid synchronous with the upward phase of the nystagmus in the left eye. The author, therefore, considers the possibility of this actually being a case of bilateral nystagmus, modified by the unilateral palsy and the severe unilateral (glaucomatous) loss of vision. (9 figures, 2 references) Peter C. Kronfeld.

Ferrata, L. **Ophthalmologic aspects of intracranial injuries.** Riv. oto-neuro-oftal. **32**:41-52, Jan.-Feb., 1957.

At the fifth congress of the Italian Society of Oto-Neuro-Ophthalmology, the subject for discussion was: Oto-Neuro-Ophthalmologic aspects of intracranial injuries. Ocular symptoms form an important part of the general picture in intracranial injuries. The author analyzes the ocular manifestations of intracranial injuries under the following headings: optic nerve, chiasm, optic tracts and lateral geniculate bodies, optic radiations, visual cortex, retinal asthenia, visual fields, papilledema, pupillary changes, and the oculomotor apparatus. (12 references) William C. Caccamise.

Pagani, Luciano. **Marcus Gunn phenomenon and its treatment.** Rassegna ital. d'ottal. **25**:208-219, May-June, 1956.

In the discussion of this neuromuscular abnormality, Pagani presents the opinions of numerous writers on this subject. He then presents the case history of a 19-year-old girl with a typical Marcus Gunn syndrome. The Blaskovics operation was performed and an almost perfect result followed. Pagani discusses the neurologic defects which explain the clinical picture. (4 figures, 46 references) Eugene M. Blake.

Pettinati, Sergio. **Roentgen therapy in optic neuritis.** Rassegna ital. d'ottal. **25**: 224-229, May-June, 1956.

The action of X-rays on various tissues and in various doses is discussed and the areas to which the rays are directed are explained. Especially favorable results of treatment are seen in the demyelinating type of optic neuritis. The rays are completely innocuous and the improvement after treatment is at times very prompt. Cases of optic neuritis due to sinusitis and to alcohol-tobacco poisoning are less influenced. Eugene M. Blake.

14

EYEBALL, ORBIT, SINUSES

Gigglberger, H. **Radiologic and ophthalmologic findings with bone tumors of the skull.** Klin. Monatsbl. f. Augenh. **130**:310-328, 1957.

Internal frontal hyperostosis and osteomas of the paranasal sinuses may cause headaches and ocular pain. The osteomas may invade the orbit. A primary hyperostosis of the sphenoid was observed. A localized osteitis fibrosa led to a remarkable enlargement of the orbit. A reticulum cell sarcoma caused multiple bony defects in the skull. Metastatic tumors to the bones of the skull, plasmocytomas and myelomas are discussed. (29 figures, 5 references) Frederick C. Blodi.

Moran, R. E. **The correction of exophthalmos and levator spasm.** Plast. & Reconstruct. Surg. **18**:411-426, Dec., 1956.

Malignant exophthalmos as lately as 1930 meant possible blindness, perhaps death. Surgical orbital decompression from the lateral approach was described by Kroenlein in 1889, and was used in 1911 by Dollinger. Moran's technique, as described in Spaethe's textbook, has been used by Moran in 33 patients. Of these, seven were male, 26 female, two were colored. Ten patients were under 30 years of age, 12 were between 30 and 40, while 11 were over 40. Twenty patients had bilateral surgery, 11 unilateral. After decompression, 12 had so much residual levator spasm, that a second surgical procedure was done. The combined aponeurosis of the lid levator and Mueller's muscle was notched from the anterior side to four-fifths of its thickness. This not only relieved the staring appearance of the eyes, but also resulted in one millimeter or more of enophthalmos. The mechanics of this levator spasm exophthalmos is described.

The cause of malignant exophthalmos remains unsolved, but Moran's observations during surgery included orbital edema, lacrimal gland edema, vascular congestion, hypertrophy of the extraocular muscles, and levator spasm. He found no increase or change in orbital fat. Paul W. Miles.

15

EYELIDS, LACRIMAL APPARATUS

Battistini, Antonio. **Chronic lupus erythematosus of the lid. Its course and its therapy.** Arch. di ottal. **60**:282-286, Sept.-Oct., 1956.

Good results were obtained in one case with Clorochina, a drug related to Atebrine. (1 figure, 6 references)

John J. Stern.

Best, W. **The pseudo-Graefe phenomenon.** Klin. Monatsbl. f. Augenh. **130**:289-296, 1957.

A 20-year-old girl had a retraction of the left upper lid when looking down and to the left. There was also paresis of the left inferior oblique muscle. The phenomenon which is usually more pronounced in the nasal field is explained on the basis of reciprocal innervation. Whenever a depressor is stimulated the levator will be inhibited. In the nasal field the depressor (the superior oblique) is innervated by the fourth cranial nerve and works against an antagonist here innervated by a paretic or damaged third nerve. Therefore, less innervation of the superior oblique is necessary and less reciprocal inhibition of the levator will result, giving the appearance of a lid retraction. (9 figures, 1 table, 53 references)

Frederick C. Blodi.

Brown, J. B. and Fryer, M. P. **Carcinoma of eyelids and canthal region.** Geriatrics **12**:181-184, March, 1957.

Surgical excision and immediate repair are desirable if local tissue is available. Basal cell carcinomas are usually found in the region of the eyelids; squamous cell carcinomas are not uncommon and usually appear as an ulcer. Treatment consists of removal of the malignant tumor, protection of the eye, and repair of the deformity resulting from the surgical removal of the tumor involved. (3 figures, 2 references) Irwin E. Gaynon.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
411 Oak Street, Cincinnati 19, Ohio

News items should reach the editor by the 10th of the month. For adequate publicity, notice of postgraduate courses and meetings should be received three months in advance.

Deaths

Dr. James Dudley Goodman, Elyria, Ohio, died February 14, 1957, aged 44 years.

Dr. William Rigby Jacobs, Lewiston, Idaho, died January 26, 1957, aged 50 years.

Dr. Abraham Mark Schwager, New York, New York, died January 25, 1957, aged 76 years.

Dr. John Herbert Waite, Boston, Massachusetts, died February 23, 1957, aged 67 years.

Dr. Joseph Roosevelt Weintrob, Atlantic City, died January 28, 1957, aged 44 years.

Pan-Pacific surgical congress

The seventh congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, November 14 through 22, 1957. All members of the profession are cordially invited to attend and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program by leading surgeons with sessions in all divisions of surgery and related fields promises to be of interest to all doctors.

Further information and brochures may be obtained by writing to:

Dr. F. J. Pinkerton
Director General of the Pan-Pacific Surgical Association
Room 230, Young Building
Honolulu, Hawaii

Colorado convention

The postgraduate course in ophthalmology and the summer convention of the Colorado Ophthalmological Society will be held July 22nd through 25th at the University of Colorado School of Medicine. Featured at the meeting will be a "Symposium on glaucoma" and a discussion of "Aids in refraction of amblyopia."

Presiding at the opening session will be Dr. James P. Rigg and Dr. Robert N. Shaffer will speak on "The glaucomas: Classification, mechanism, diagnostic procedures," and Dr. Robert A. Schimek on "Principles of gonioscopy." Dr. Thomas M. Van Bergen will preside at the afternoon session at which Dr. H. Saul Sugar will discuss "Congenital and secondary glaucoma," and Dr. Arthur Linksz, "Refraction and optical aids in reduced vision."

The second day's session will open with a paper by Dr. Sugar on "Narrow-angle glaucoma," and one by Dr. Shaffer on "Wide-angle glaucoma," Dr. William H. Droegemueller presiding. Dr. William K. Kuhlman will preside over the session of the third morning at which Dr. Linksz will discuss "Refraction and optical aids in reduced vision."

On Wednesday afternoon, Dr. George A. Filmer presiding, there will be a round-table discussion period moderated by Dr. Linksz, Dr. Schimek, Dr. Shaffer, and Dr. Sugar, and Dr. Schimek will present a paper on "Simplified tonography."

Thursday morning's session will be presided over by Dr. James C. Strong, Jr., and the speakers are Dr. Shaffer, Dr. Sugar, and Dr. Schimek who will discuss "Medical treatment of glaucoma," "Surgical treatment of glaucoma," and "Iridencleisis and cyclodialysis." Movies will be shown.

British Columbia conference

The first British Columbia Oto-Ophthalmological conference, held in Vancouver on May 22nd to 25th, was well attended by doctors of the Pacific Northwest.

Dr. Alston Callahan of Birmingham, Alabama, gave several lectures on "lid plastic surgery" which were copiously and beautifully illustrated by movies. The guest speaker was Sir Victor Negus of London, England.

Irish Ophthalmological Society

Dr. Frank B. Walsh, Baltimore, presented the Montgomery Lecture before the Irish Ophthalmological Society and their guests, the Society of British Neurological Surgeons, at the society's 36th annual meeting held in Dublin during May. The subject of Dr. Walsh's address was "Third-nerve regeneration: Clinical evaluation."

Other speakers on the program were: Dr. Alan Mooney, president of the society, "Some neuro-ophthalmological problems"; Dr. Max Chamlin, New York, "Visual field changes produced by X-ray treatment of pituitary tumors"; Prof. Sir Geoffrey Jefferson, Dr. Pollak, and Dr. P. O. Yates, Manchester, "Invasion of the optic chiasma and optic nerves by neighboring gliomas."

Dr. Uhlein, Mayo Clinic, "Acute visual failure as a neurosurgical emergency"; Mr. M. J. Roper-Hall, Birmingham, "Optic disc edema without raised intracranial pressure"; Prof. Scott and Prof. Dott, Edinburgh, "The ocular aspects of endocrine exophthalmos"; Prof. Krayenbuhl, Zurich, "The diagnostic value of orbital angiography."

Mr. Murray Falconer, London, "The extent of visual field defects following anterior temporal lobectomy"; Mr. Harvey Jackson, London "Pseudotumors of the orbit"; Mr. P. C. Carey, London, "Epidermoids of the orbit"; Mr. Alan Kerr, Liverpool, "Hormone replacement therapy in cases of

craniopharyngioma"; Mr. E. J. Newton, Birmingham, "Some problems presented by hematogenous brain abscess."

Dr. MacDougald, "The detection of glaucoma"; Mr. H. B. Stallard, London, "Anterior flap sclerotomy with basal iridencleisis"; Dr. F. D. McAuley, "Technique and results of retinal detachment surgery using binocular indirect ophthalmoscopy."

During the meeting a symposium on "The blood supply of the chiasma and optic nerves in relation to visual field defects," was presented, with Prof. François, Ghent, Prof. Erskine, and Prof. Brodie Hughes, Birmingham, as opening speakers.

Brooklyn meeting

Dr. Agnes Griffin and Dr. Martin Bodian presented a paper on "Segmental retinal periarteritis," at the 143rd regular meeting of the Brooklyn Ophthalmological Society.

Nassau meeting

Dr. Graham Clark presented a paper on "Retinal detachment," at the April meeting of the Nassau (county) Ophthalmological Society, held at Hempstead, Long Island.

Kentucky society

The Kentucky Eye, Ear, Nose, and Throat Society will meet jointly with the Kentucky State Medical Society in Louisville, Kentucky, on September 18, 1957. The guest speakers will be Dr. Donald Shafer, New York, who will speak on "Vitreous implants in retinal detachment surgery," and Dr. Floyd J. Putney, Philadelphia, whose subject will be "Surgery of the neck."

Miscellaneous

Gill meeting

Forty-two states and five foreign countries were represented at the 30th annual spring congress of the Gill Memorial Eye, Ear, and Throat Hospital, Roanoke, Virginia. There were 18 guest speakers and 60 lectures. The 1958 congress will be held April 14th through April 19th.

Sibley hospital

Dr. John M. Orem, president of the Board of Trustees of Sibley Memorial Hospital, Washington, D.C., announced establishment of two new departments for the proposed new Sibley Hospital for which a $1,500,000 fund drive is now under way.

The two new units, not originally contemplated in building plans, are a Department of Ophthalmology under Dr. William M. Hart, Bethesda, Maryland, and a Department of Psychiatry under Dr. Zigmond M. Lebensohn, Washington.

Sibley Memorial Hospital, which will be a 350-bed hospital and has become an integral part of The American University, Nebraska and Massachusetts Avenues, will design the entire seventh floor of its new building to the two projected units.

Dr. Hart said his eye-treatment section will have 30 beds, plus a clinic for out-patients. The arrangement will make possible a training program for eye surgeons, he added. Dr. Hart, an associate professor at Georgetown University and consultant in ophthalmology at Walter Reed Army Institute of Research, lives in Springfield, Virginia, although most of his work is in Bethesda.

Personals

Dr. Alan C. Woods, Baltimore, is to receive the Gonin Medal at the XVIII International Congress of Ophthalmology to be held in Brussels in 1958.

Dr. Roland I. Pritikin, Rockford, Illinois, while at Shikarpur, W. Pakistan, earlier this year was named president of the Henry Holland Hospitals Alumni Association and of the Henry Holland Mission Hospitals Fund. All alumni of the Eye Hospitals of Shikapur and Khairpur Mirs are urged to remit an annual subscription of one dollar or more to Dr. Victor E. Lepisto, 238 Quincy Street, Hancock, Michigan, treasurer.

Dr. L. P. Agarwal has been appointed reader of ophthalmology and head of the Department of Ophthalmology, Medical College, Kanpur (U.P.), India.

Mr. A. J. B. Goldsmith, F.R.C.S., was a visiting professor of ophthalmology at the University of Toronto for the month of May, 1957, as exchange lecturer from the Middlesex Hospital, London, England.

Dr. Gordon M. Bruce, New York, has been appointed to represent ophthalmology on the Board of Reserve Consultants to the Bureau of Medicine and Surgery, U. S. Navy.

Dr. Donald J. Lyle, professor and chairman of the Department of Ophthalmology at the medical college of the University of Cincinnati, delivered the Moynihan Lecture before the Royal College of Surgeons, London, on May 8th. He spoke on the "Causes and treatment of exophthalmos."

Dr. John S. McGavic, professor of ophthalmology, Temple University Medical Center, spoke on, "Complications of glaucoma surgery" in Washington, D.C., recently. He also delivered a paper entitled "Chronic granulomatous inflammation of the eye: Case presentation," before a meeting of the Ophthalmic Pathology Club in Washington, D.C.

E. B. Meyrowitz

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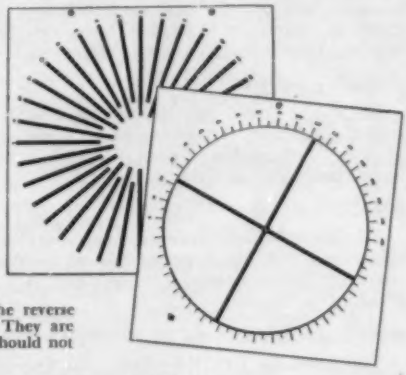

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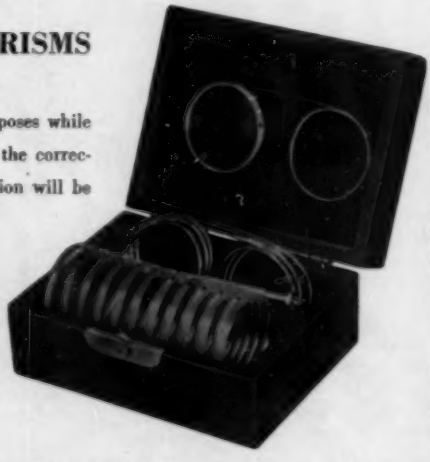

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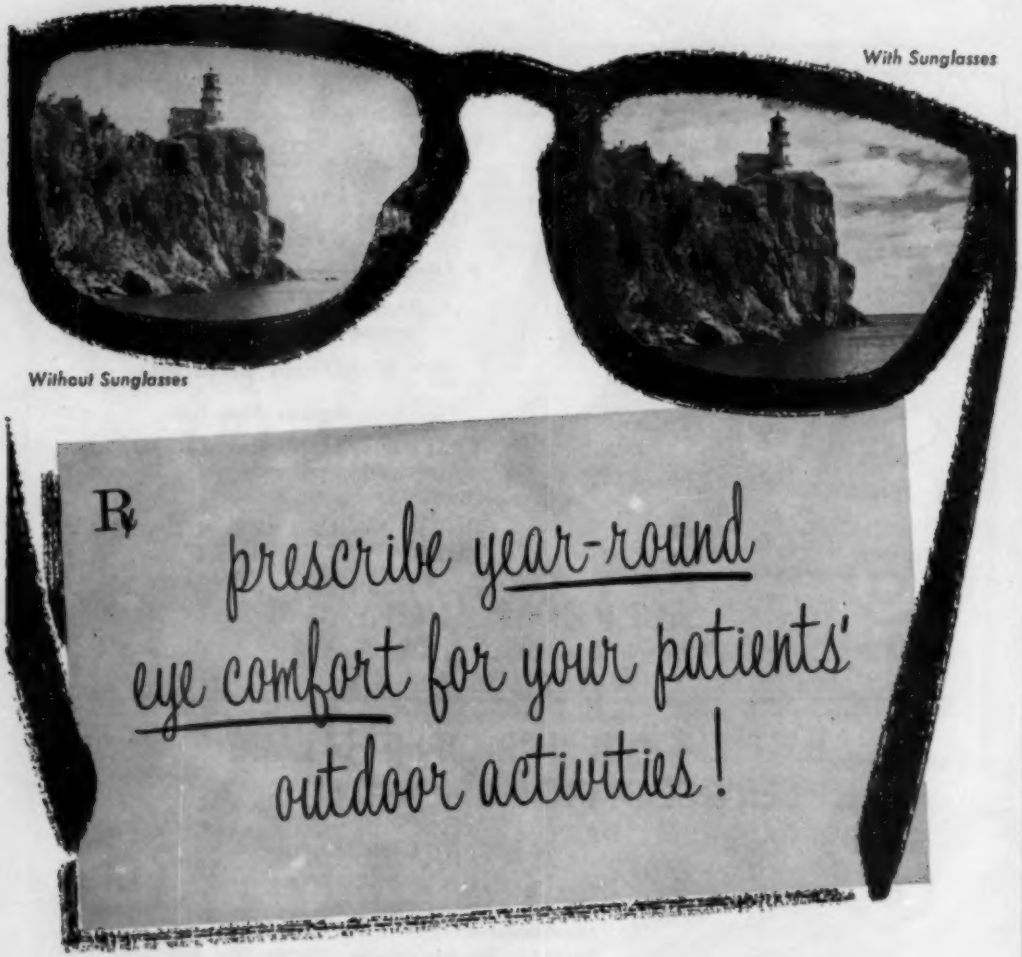

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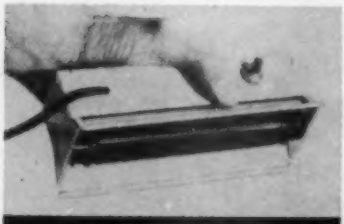

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